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CONTENTS.

PAGE

The Cultivation of Tubercle Bacilli from the Circulating Blood in Miliary Tuberculosis. By Mildred C. Clough, M. D. 363

Fibroid Tumors of the Vulva. A Report of 12 Cases and a Digest of the Literature on the Subject. (Illustrated.) By V. N. Leonard, M. D. 373

Books Received 385

Index 387

THE CULTIVATION OF TUBERCLE BACILLI FROM THE CIRCULATING BLOOD IN MILIARY TUBERCULOSIS.*

By Mildred C. Clough, M. D.

(From the Medical Clinic of The Johns Hopkins Hospital.)

The occurrence of tubercle bacilli in the circulating blood in miliary tuberculosis has been recognized for a long time. The pathological anatomy of this disease indicates that tubercle bacilli must be distributed throughout the body from a primary focus by way of the blood stream. Even before the discovery of the tubercle bacillus, Villemin in 1868, and later others, produced tuberculosis in animals by inoculation with blood, first from experimentally infected animals, and later from tuberculous patients. Since that time, the presence of tubercle bacilli in the circulating blood of tuberculous patients has been proven by many investigators by the production of generalized tuberculosis in guinea-pigs inoculated with blood. The results obtained by a number of different authors are summarized in Table I.

As is shown in the table, there is a great discrepancy in the percentage of positive results obtained by different authors from the inoculation of guinea-pigs with blood. This may be explained in two ways.

First, in some cases, the diagnosis of tuberculosis in the inoculated guinea-pigs is unreliable. For example, in the series reported by Liebermeister many of the guinea-pigs reported as tuberculous died in from one to three weeks (or even less) after inoculation, obviously of an acute intercurrent infection, without distinctively tuberculous lesions. No histological studies were reported, and the diagnosis was based on staining acid-fast rods in smears from the bloody peritoneal exudate or from the organs. Some authors, for instance Kennerknecht, considered a guinea-pig tuberculous in the absence of gross lesions or histological changes if they found acid-fast bacilli in the blood of the animal, or even in the sediment from the organs when digested with antiformin. Sturm even went so far as to call a guinea-pig tuberculous because he was able to find Gram-positive bacilli and Much granules in the sediment of the digested organs. In other reports, including those of Haga, Klemperer, and C. Fraenkel, the character of the lesions found in the inoculated animals is not described, and it is impossible to draw any conclusions as to the reliability of the results.

Secondly, the type of cases studied differs in the different reports, some authors including only miliary tuberculosis in their statistics, and others only pulmonary or other types of tuberculosis. In this table the cases of miliary tuberculosis reported are separated from tuberculosis of other types, and included under a different heading.

In all, I have collected from the literature 1508 cases of tuberculosis studied by guinea-pig inoculation, of which 195 gave positive results. The percentage of positive results (12.9 per cent) in this series corresponds approximately to that obtained by Fischer in a compilation of 1250 cases with 17 per cent positive inoculations, by Fraenkel of 500 cases with 20 per cent positive results, and by Austrian and Hamman of 863 cases with 11 per cent positive inoculations. My figures are undoubtedly too high, because included in my table are

* This work was done under the Mary Putnam Jacobi Fellowship of The Woman's Medical Association of New York City.

TABLE I.—GUINEA-PIG INOCULATIONS WITH BLOOD FROM TUBERCULOUS PATIENTS.

Name.	Date.	Total cases.	No. +.	% +.	No. of miliary cases.	No. +.	% +.	Ante or post mortem.	Amount of blood injected.	Type of tuberculous lesion produced.	Remarks.
Meisel	1884	8	8	100	8	8	100	1 A. M. 7 P. M.	Small amt. of clot.	Gross lesions.	
Kühnau	1897	12	1	8	4	1	25	A. M.	.....	Not stated.	
Jousset	1903	6	2	33	0	0	0	A. M.	.....		
Bergeron	1904	26	1	4	2	1	50	A. M.	5–10 c.c.		
Gary	1905	16	5	31	1	1	100	A. M.	.....	All gross lesions.	
Lüdke	1906	14	5	35	2	2	100	A. M.	5–10 c.c.	Gross lesions. Tubercle bacilli stained in organs.	3 positive cases in advanced pulmonary tuberculosis.
Huguenin	1908	1	1	100	0	0	0	P. M.	.....	.....	Blood of a fœtus.
Anderson	1909	48	0	0	0	0	0	A. M.	2½ c.c.	.....	47 pulmonary cases with bacilli in sputum. One joint case. Parallel cultures negative.
Dailey	1909	17	0	0	2	0	0	A. M.	1–2 c.c.		
Liebermeister	1909	50	20(?)	40	0	0	0	A. M.	3–6 c.c.	Questionable gross lesions. Diagnosis in many cases depends on staining bacilli in peritoneal exudate.	Pulmonary cases.
Sturm	1911	50	23(?)	46	0	0	0	A. M.	5 c.c.	Gross lesions in a few cases. Many results based on staining bacilli in sediment of digested organs. 3 cases seem certainly, and 4 probably positive.	
Fraenkel, C.	1912	50	7	14	0	0	0	A. M.	.....	.....	Pulmonary cases.
Bacmeister and Reuben	1912	15	0	0	0	0	0	A. M.	.....	.....	Incipient pulmonary cases.
Kennerknecht	1912	13	13(?)	100	0	0	0	A. M.	Not given.	Some gross lesions. Diagnosis mainly depended on staining bacilli in blood or organs of guinea-pigs.	
Liebermeister	1912	50	20(?)	40	0	0	0	A. M.	3–6 c.c.	No protocols.	Reports 100 cases with 40 positive results, including 50 already listed (1909).
Nobécourt and Darré	1912	40	4	10	2	2	100	.....	10–20 c.c. in 2–3 pigs.	.....	1 case tuberculous meningitis +. 1 case acute tuberculous bronchopneumonia +.
Rumpf	1912	35	3	9	0	0	0	A. M.	Not given.	Not stated.	
de Amicis	1913	30	0	0	0	0	0	A. M.	5–9 c.c.	.....	Tuberculosis of lungs, glands, peritoneum, pleura, kidneys.
Bacmeister	1913	15	4	27	0	0	0	A. M.	10 c.c.	Gross lesions and stained smears.	4 positive only after a tuberculin reaction.
Bernard et al.	1913	2	2	100	2	2	100	.....	.....		
Bogasau	1913	41	0	0	0	0	0	A. M.	Not stated.	.....	"Phthisis" cases.
Dreesen	1913	36	1	3	0	0	0	A. M.	.....	.....	Also 30 normals—all negative. Positive case, advanced phthisis.
Elsässer	1913	25	0	0	0	0	0	A. M.	.....	.....	All pulmonary cases.
Fraenkel, E.	1913	24	2	8	0	0	0	A. M.	Not stated.	Gross lesions and stained smears.	All pulmonary cases.
Haga	1913	81	24	30	0	0	0	A. M.	1–2.5 c.c. in 4 pigs.	Not stated.	
Kachel	1913	26	4	15	0	0	0	A. M.	4–5 c.c.	Gross lesions not extensive.	One other pig gave a + tuberculin reaction.

TABLE I.—GUINEA-PIG INOCULATIONS WITH BLOOD FROM TUBERCULOUS PATIENTS.—CONTINUED.

Name.	Date.	Total cases.	No. +.	% +.	No. of miliary cases.	No. +.	% +.	Ante or post mortem.	Amount of blood injected.	Type of tuberculous lesion produced.	Remarks.
Lange and Lindemann.	1913	78	1	1	0	0	0	A. M.	.....	Not stated.	Animal experiments not completed.
Mayer.....	1913	25	0	0	1	0	0	A. M.	Not stated.	.....	24 pulmonary cases.
Querner.....	1913	37	0	0	0	0	0	A. M.	10 c.c.	.....	All pulmonary.
Rist et al.....	1913	50	0	0	..	..	...	.....	.....		
Rothacker and Charon.	1913	46	1	2	1	1	100	A. M.	3 c.c.	Gross lesions.	Several advanced pulmonary cases.
de Verbizier	1913	15	0	0	0	0	0	A. M.	Sediment of 5 c.c.		
Baetge	1914	29	8	27	0	0	0	A. M.	6 c.c. each in 2 pigs.	Not stated.	28 pulmonary, 1 meningitis negative. Only 1 of each pair of pigs died.
Fischer.....	1914	13	0	0	2	0	0	A. M.	1–4 c.c.	.....	2 miliary cases probably chiefly meningeal.
Haas.....	1914	24	0	0	0	0	0	A. M.	6–7 c.c.	.....	Surgical cases.
Klemperer.....	1914	25	6	24	2	2	100	A. M.	5 c.c.	Not stated.	16 pulmonary cases—2+. 1 pleurisy twice +; recovery.
Klopstock and Seligmann	1914	49	0	0	0	0	0	A. M.	2 c.c. in each of 2 pigs.	Gross and microscopic.	
Lehmann	1914	104	6	6	2	1	50	A. M.	1–2 c.c.	Gross lesions.	1 tuberculosis of cheek and hand +. 1 scrofula and healed bone tuberculosis +. 2 occult tuberculosis +. 1 pulmonary tuberculosis +.
Rautenberg.....	1914	5	0	0	0	0	0	A. M.	5 c.c.	Injected apes and guinea-pigs.	Advanced pulmonary cases.
Seidenberger and Seitz	1914	26	9	35	7	6	85	P. M.	5 c.c.	Gross lesions.	
Storath	1914	17	0	0	0	0	0	A. M.	5–10 c.c.	Gross and microscopic. All rabbits.	Before and after tuberculin.
Austrian.....	1915	25	0	0	0	0	0	A. M.	4–7½ c.c.	.....	Pulmonary cases.
Hamman	1915	20	0	0	0	0	0	A. M.	2½–5 c.c.	.....	Pulmonary cases.
Brown et al.....	1915	84	3	4	0	0	0	A. M.	8–10 c.c.	Gross lesions.	Pulmonary cases.
Moewes.....	1915	80	9	11	10	5	50	1, P. M. 79, A. M.	2½–3¾ c.c. Some 20 c.c.	Not given.	10 miliary cases. 70 pulmonary cases.
Rumpf and Zeissler	1915	25	2	8	0	0	0	.....	Not stated.	Histological lesions.	Pulmonary cases.
Total.....	.....	1508	195	12.9	48	32	66.6	.....	.....		

the results of several investigators who were not sufficiently critical in their interpretation of tuberculous lesions in guinea-pigs. If the series of Liebermeister, Sturm, and Kennerknecht are omitted, there remain 1345 cases with 119 positive inoculations, approximately 8.8 per cent. Faber, selecting 1060 cases tested by guinea-pig inoculation with blood obtained during life, found only 4.2 per cent positive, while in 37 cases tested post mortem 38 per cent were positive.

If one considers only cases of miliary tuberculosis the percentage of positive guinea-pig inoculations with blood becomes much higher. Of 48 cases of miliary tuberculosis listed in Table I 32 gave positive results, or 66.6 per cent. These figures are probably reliable, because in nearly all instances gross lesions were reported in the inoculated animals. If the cases of miliary tuberculosis are subtracted from the total number, there remain 1297 cases with 87 positive inoculations, a percentage of 6.7 for all types of tuberculosis other than miliary tuberculosis.

One may conclude, therefore, that the occurrence of tubercle bacilli in the circulating blood, at least in sufficient number to infect a guinea-pig, is relatively infrequent (6.7 per cent) in all forms of tuberculosis other than miliary tuberculosis, whereas in miliary tuberculosis, tubercle bacilli occur in the blood in a large percentage (66.6 per cent) of cases.

The attempted demonstration of tubercle bacilli in the blood by means of stained smears needs little comment. Austrian and Hamman in 1915 published a detailed article with a fairly complete bibliography on the subject, and Berry in her article has good summaries of the earlier literature. Liebmann in 1891 reported the finding of tubercle bacilli in blood smears from tuberculin-treated patients. It was shown, however, that his findings were due to gross errors in technique.

Interest in the subject was reawakened in 1909, by the publications of Rosenberger in this country and of Schnitter in Germany. Rosenberger reported the demonstration of tubercle bacilli in the blood in 100 per cent of a series of 49 cases, and later of 300 cases, by staining the organisms in the centrifugalized sediment from citrated blood. Schnitter used a modification of Stäubli's acetic-acid method for the demonstration of parasites in the blood. After hemolyzing the red blood cells in acetic-acid he digested the sediment, obtained by centrifugalization, with antiformin. He claimed to have found tubercle bacilli in smears from the sediment so obtained in 32 per cent of tuberculous cases.

Following these publications a large amount of work was done on the subject with very conflicting results. Kurashige even found tubercle bacilli in blood from apparently normal persons. Parallel experiments with guinea-pig inoculations and staining methods did not, in most instances, give corresponding results. A source of error in these results was pointed out first by Brem, who demonstrated the frequent presence of acid-fast bacilli in distilled water. This observation was later confirmed by other writers (Burvill-Holmes, Beitzke, A. Lehmann). Bacmeister and Reuben found that the chemical reaction of acetic acid and antiformin may cause appearances simulating acid-fast bacilli, and Bernard, Debré, and Baron found acid-fast granules in pure antiformin. These observations, together with the conflicting results obtained from parallel series of guinea-pig inoculations, indicate the unreliability of the method.

The frequent difficulty in the differential diagnosis of miliary tuberculosis from other non-tuberculous infections clinically, and the slowness and uncertainty of diagnosis by guinea-pig inoculation, suggested the use of cultural methods for the demonstration of tubercle bacilli in the blood.

A fairly extensive review of the literature reveals only one case in which tubercle bacilli have been cultivated from the blood of tuberculous patients. This was a case reported by Faber, who obtained a growth of tubercle bacilli on a plain agar slant inoculated with blood from the heart of a child dead of generalized tuberculosis. Faber obtained negative cultures with 1 to 5 c. c. of blood in 21 other cases of miliary tuberculosis in children, and negative cultures have been obtained from the blood by Brown, Heise, and Petroff in 22 pulmonary cases, and by Anderson in 47 pulmonary cases and one joint case. Positive cultures from the blood of experimentally infected guinea-pigs and rabbits have been reported by Loewenstein, and later by Anderson.

The following method, suggested by Dr. Paul W. Clough, was used at first in my cultures, but was later modified in order to decrease the time necessary for growth to become apparent. Ten to 15 c. c. of blood were aspirated with a syringe from a cubital vein and added to an equal volume of 1½ per cent solution of sodium citrate to prevent clotting. Part of this blood was used to control guinea-pig inoculations in most of the cases. The remaining blood was added to shallow flasks of 5 per cent glycerine broth made neutral or slightly acid (phenolphthalein). After a preliminary incubation the contents of the flasks were centrifugalized and the sediment planted on blood-agar slants. Human blood agar was used because it was simply and easily obtained. The slants were then sealed with paraffine to prevent drying, and incubated.

Positive results were obtained by this method in three cases.

Case 1.—G. H. (Med. No. 23207), colored boy, 5 years of age. A clinical diagnosis of acute miliary tuberculosis was made, though at first the clinical picture resembled that of typhoid fever. Autopsy diagnosis: Acute miliary tuberculosis with the primary focus in the mediastinal glands, rupturing into the azygos vein. The blood culture was obtained 10 days before death. Three c. c. of citrated blood were added to a flask of glycerine broth and incubated for six weeks. Smears made from the sediment in the flask at this time showed acid-fast bacilli. The contents of the flask were then centrifugalized, part of the sediment planted on blood-agar slants, and part injected intraperitoneally into each of two guinea-pigs. After three weeks a dry, wrinkled, slightly brownish growth was noted on the blood-agar slants, and after six weeks one of the guinea-pigs died with generalized tuberculosis. Tubercle bacilli were demonstrated in smears from the subcultures, and from the organs of the guinea-pig, and were grown in culture from the spleen and liver of the guinea-pig. The other guinea-pig, inoculated with the sediment, died four days after the injection without tuberculous lesions.*

Case 2.—G. W. (Med No. 35610), white man, 37 years of age. In this case also the clinical picture at first resembled that of typhoid fever, but the subsequent course made a definite diagnosis of miliary tuberculosis possible. Autopsy diagnosis: Fibrinous pleurisy, encapsulated apical pulmonary tuberculosis, bronchial lymphadenitis, caseous tuberculosis of the left adrenal, caseous mesenteric and retroperitoneal tuberculosis, rupture of a caseous gland into the cisterna chyli, generalized miliary tuberculosis, tuberculous meningitis and choroiditis, ulcer of the ileum. Fifteen c. c. of blood were obtained in citrate solution 14 days before death. A guinea-pig inoculated intraperitoneally with 3 c. c. of the blood died a few days later without tuberculous lesions. Twelve c. c.; of the blood were added to several flasks of glycerine broth, and incubated for about five weeks. The contents of the flasks were centrifugalized, and the sediment planted on blood-agar slants which were then sealed. About four weeks later numerous pin-head-sized, buff-colored, dry colonies were noticed. Smears from the culture showed slender, acid-fast bacilli, some curved and beaded, typical of the tubercle bacillus in their morphology and arrangement. Three guinea-pigs were injected with varying amounts of the culture, and all developed generalized tuberculosis. At autopsy all of the animals showed caseous tissue at the points of inoculation, extensive glandular enlargement with caseation in many of the glands, and caseous conglomerate tubercles in the spleens, which in two of the guinea-pigs were six to eight times the normal size. Two of the guinea-pigs showed also similar caseous tubercles in the liver. Typical tubercle bacilli were demonstrated in the glands, spleens, and livers of all the inoculated guinea-pigs. Subcultures from the original culture were made, and a characteristic growth appeared in about 10 days. Smears from this growth showed typical tubercle bacilli in pure culture.

Case 3.—J. E. (H. L. H. Disp. No. 12893), white boy, 6 years of age, from the service of Dr. Howland. Clinical diagnosis: Acute generalized miliary tuberculosis, tuberculous meningitis, and tuber-

* This blood culture, and several of the cultures from other fluids included in Table II, were taken by Dr. Paul W. Clough, and the data in regard to them obtained, with his permission, from the hospital records.

culosis of the choroid. No autopsy was made. X-ray examination showed miliary tuberculosis of the lungs. Tubercle bacilli were demonstrated by smears and by guinea-pig inoculation in the spinal fluid. The blood culture was made three days before death. Fifteen c. c. of blood were obtained in citrate solution. Two guinea-pigs were inoculated in the left groin with 3¾ c. c. of blood each. One guinea-pig lived four months and when killed at the end of that time, showed no tuberculous lesions. The other guinea-pig remained healthy for four months and was then lost. The other half of the blood (7½ c. c.) was added to shallow, glycerine, broth flasks. After 16 days the contents of the flasks were centrifugalized, the sediment planted on blood-agar slants and the slants sealed. This culture was set aside after a short period of observation, and was not looked at again until six months later, when a growth was noticed on one slant in the water of condensation. Characteristic, large, buff-colored, dry colonies were present in the fluid, and also at the base of the slant where the water of condensation had washed over the slant. Smears from the growth showed an acid-fast bacillus having the morphological features of the tubercle bacillus. An emulsion made from the growth was injected into two guinea-pigs. One of these died 18 days later with a large caseous mass at the site of inoculation, enlarged but not caseous iliac, mesenteric, and bronchial glands, marked enlargement of the spleen which was studded with miliary tubercles, and consolidation of the left lung. Typical tubercle bacilli were demonstrated in smears from the spleen. The other guinea-pig died six weeks after inoculation with caseation at the point of injection, general glandular enlargement with caseation, and extensive miliary tuberculosis of the spleen and liver. Smears from the liver and spleen showed many tubercle bacilli. Subcultures from the original culture were made, and a typical growth appeared in about nine days.

In carrying out these cultures no attempt was made to make an early diagnosis of the cases by means of the cultures, and they were not watched carefully for the first appearance of growth. In order to make the cultures of practical value in diagnosis it seemed desirable to try methods which would yield growth in a shorter period of time. In the third case cited above, the appearance of growth in only one of the slants inoculated from the broth after 16 days incubation suggested that very little multiplication had occurred in the broth. It was thought, then, that this preliminary incubation in broth might be dispensed with, and the following method was used. The blood was hemolyzed with distilled water, and the sediment after centrifugalization planted directly on blood agar slants which were sealed with paraffine.

Since there were no cases of miliary tuberculosis in the clinic at the time, the experiment was made with normal blood artificially seeded with a very small number of tubercle bacilli (G. W., third transfer). Ten cubic centimeters of blood were collected in the usual way, and the red blood corpuscles hemolyzed by the addition of distilled water. The blood was then centrifugalized at high speed for 1½ hours, and the sediment planted on blood-agar slants which were sealed with paraffine. In six days growth became visible as small, semi-transparent colonies, which in eight days were somewhat larger and more opaque, and at the end of 10 days were characteristic. Growth in the culture direct from the body would probably have been somewhat slower in appearing than in this culture from the third transfer. Smears from the culture showed tubercle bacilli in pure culture.

Three positive cultures were obtained by the second method in two cases. In one of these cases two positive blood cultures were obtained, one ante mortem, and one from the heart's blood post mortem.

CASE 1.—E. M. (H. L. H. Disp. No. 14950), colored girl, 8 years of age, from the service of Dr. Howland. Clinical diagnosis: Generalized miliary tuberculosis, tuberculous meningitis. Autopsy diagnosis: Generalized tuberculous lymphadenitis, generalized miliary tuberculosis, tuberculous meningitis and peritonitis. Focus of dissemination not found. A blood culture was obtained one day before death. Twenty c. c. of citrated blood were hemolyzed by the addition of distilled water. The blood was then centrifugalized and four-fifths of the sediment (representing 16 c. c. of blood) was planted on blood agar slants. One-fifth of the sediment (from 4 c. c. of blood) was injected subcutaneously into the groin of a guinea-pig. This animal died three months later from an intercurrent bronchopneumonia without tuberculous lesions. In this case hemolysis of the blood was incomplete, and the slants were covered with a rather thick layer of sediment. For this reason growth did not become evident for 25 days. Smears from this growth showed typical tubercle bacilli. A guinea-pig inoculated with a suspension of this growth died 10 weeks later, and showed a general glandular enlargement with caseation in many of the glands, and a marked enlargement of the spleen, which was full of tubercles. The nature of these lesions was confirmed by microscopical sections. Tubercle bacilli were grown from the spinal fluid in this case in 10 days.

CASE 2.—Ten c. c. of blood were obtained from the heart of the preceding case at autopsy, and cultured in the same way. Growth became evident 13 days after the culture was made as small, colorless, non-characteristic colonies, and smears from the culture showed numerous tubercle bacilli. The spinal fluid obtained post mortem was also cultured. After 13 days growth was noted as fair-sized, buff-colored, dry, rounded colonies.

CASE 3.—L. M. (H. L. H. Disp. No. 15068), white girl, 4 years of age, from the service of Dr. Howland. Clinical diagnosis: Pulmonary tuberculosis, tuberculous meningitis, miliary tuberculosis (?). No autopsy was obtained. The blood was cultured one day before death. Ten c. c. of blood were obtained in citrate solution, and the red blood cells laked by the addition of distilled water. After centrifugalization three-quarters of the sediment was planted on blood-agar slants which were then sealed, and one-quarter of the sediment inoculated subcutaneously into the groin of a guinea-pig. After a week's incubation, minute, semi-transparent, colorless colonies became visible on some of the slants, and smears from these colonies showed clumps of typical tubercle bacilli. The guinea-pig inoculated with one-quarter of the sediment died 5½ weeks later, and showed caseous areas in the regional and iliac glands. Tubercle bacilli were demonstrated in smears from these glands. A guinea-pig inoculated with a suspension of the growth is still alive after three weeks, but shows marked enlargement of the regional glands. An exploratory operation showed extensive caseation of the regional glands, and marked enlargement of the spleen, which was firm and apparently studded with small tubercles. The spinal fluid from this case was also cultured, and definite colonies appeared in a week.

By this method of cultivation positive results have been obtained from the blood in a relatively short time in two cases. A tentative diagnosis might have been made even before the appearance of visible growth by means of smears, if sufficient multiplication had occurred. When the colonies first appear they are not characteristic, and smears must be made before an absolute diagnosis can be made. It may be a long time before the growth becomes as profuse as that of old labora-

TABLE II.—CULTURES FROM TUBERCULOUS FLUIDS.

BLOOD CULTURES.

Name.	Hospital No.	Age.	Diagnosis.	Autopsy.	Smears.	Culture. Result and interval.	Guinea-pig inoculation. Result and interval.	Remarks.
G. H.	Med. No. 23207	5	Miliary tuberculosis.	Yes.	Not done.	+. 2½ mos.	Not done.	Guinea-pig inoculated with culture developed tuberculosis. 1 guinea-pig died prematurely.
G. W.	Med. No. 35610	37	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 2½ mos.	Done. Guinea-pig died prematurely.	Guinea-pig inoculated with culture developed tuberculosis.
J. E.	H. L. H. Disp. No. 12893	6	Miliary tuberculosis. Tuberculous meningitis.	No.	Not done.	+. 5 mos.	0. 2 guinea-pigs inoculated. Both remained well.	Guinea-pig inoculated with culture developed tuberculosis.
E. M.	H. L. H. Disp. No. 14950	8	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 25 days.	0. 1 guinea-pig inoculated. Died after 3 mos. without tuberculous lesions.	Guinea-pig inoculated with culture developed tuberculosis. Spinal fluid culture +.
E. M.	H. L. H. Disp. No. 14950	8	Miliary tuberculosis. Tuberculous meningitis.	Yes.	Not done.	+. 13 days.	Not done.	Blood culture made post mortem. Spinal fluid culture +.
L. M.	H. L. H. Disp. No. 15068	4	Miliary tuberculosis. Tuberculous meningitis.	No.	Not done.	+. 7 days.	+. 5½ weeks.	Guinea-pig inoculated with culture developed tuberculosis. Spinal fluid culture +.
H. L.	H. L. H. Disp. No. 14215	7 mos.	Miliary tuberculosis. Tuberculous meningitis. Pulmonary tuberculosis.	Yes.	Not done.	0.	0. Guinea-pig well after 5 mos.	Only 2 c.c. of blood obtained. Spinal fluid culture +.
S. Ht.	Med. No. 23684	26	Miliary tuberculosis. Tuberculous meningitis. Pulmonary tuberculosis.	Yes.	0.	0.	0.	Spinal fluid culture +.
W. S.	Med. No. 36896	18	Tuberculous peritonitis.	Yes.	Not done.	0.	Not done.	
E. L.	Med. No. 24140	5	Pulmonary tuberculosis. Tuberculous adenitis.	No.	Not done.	0.	Not done.	
C. M.	Med. No. 23487	24	Pulmonary tuberculosis.	No.	Not done.	0.	Not done.	
W. M.	Med. No. 23576	23	Pulmonary tuberculosis.	Yes.	Not done.	0.	Not done.	Spinal fluid culture 0.
M. S.	H. L. H. Disp. No. 13349	3	Tuberculous meningitis.	Yes.	Not done.	0.	0.	Few old tubercles in organs at autopsy.
C. T.	Med. No. 24277	8	Tuberculous meningitis.	Yes.	Not done.	0.	Not done.	Spinal fluid culture +.
M. H.	Med. No. 23799	20	Tuberculous meningitis.	Yes.	Not done.	0.	0.	Spinal fluid culture 0.
S. Hn.	Med. No. 23508	5	Tuberculous meningitis.	No.	Not done.	0.	0.	Spinal fluid culture +.
J. J.	H. L. H. Disp. No. 15178	1	Pulmonary tuberculosis. Tuberculous meningitis.	No.	Not done.	0.	0.	Spinal fluid culture +.

PLEURAL FLUIDS.

D. M.	Med. No. 23118	21	Pleurisy with effusion. Pulmonary tuberculosis (?).	No.	0.	+. 2 mos.	+. 2 mos.	
D. K.	Med. No. 23144	13	Pleurisy with effusion. Pulmonary tuberculosis (?).	No.	0.	0.	0.	
J. C.	Med. No. 23167	35	Pleurisy with effusion.	No.	0.	0.	0.	
A. S.	Med. No. 23365	51	Pleurisy with effusion.	No.	Not done.	0.	0.	

PERICARDIAL FLUIDS.

J. L.	Med. No. 23393	33	Syphilis of aorta with multiple aneurisms. Chronic adhesive pericarditis. Pleurisy with effusion, etc.	Yes.	.....	0.	0.	Probably not tuberculous.

TABLE II.—CULTURES FROM TUBERCULOUS FLUIDS.—CONTINUED.

SPINAL FLUIDS.

Name.	Hospital No.	Age.	Diagnosis.	Autopsy.	Smears.	Culture. Result and interval.	Guinea-pig inoculation. Result and interval.	Remarks.
S. Hn.	Med. No. 23508	5	Tuberculous meningitis.	No.	Not done.	+. 5 wks.	Not recorded.	One 0 and 2 + cultures.
S. Ht.	Med. No. 23684	26	Miliary tuberculosis. Tuberculous meningitis.	Yes.	+.	+. 5 wks.	+.	2 + cultures. Blood culture 0.
M. L.	Med. No. 23922	2	Tuberculous meningitis.	No.	Not done.	+. 4 wks.	Not done.	
J. F.	Med. No. 24005	2	Tuberculous meningitis.	No.	+ later.	+. 3–4 wks.	Not done.	First culture 0. 2 + cultures.
B. A.	Med. No. 24036	8	Tuberculous meningitis.	Yes.	Twice 0.	+. 3 mos.	Not done.	2 + cultures.
O. H.	Med. No. 24110	17	Tuberculous meningitis. Miliary tuberculosis. Tuberculosis of spine.	Yes.	0.	+. 2 mos.	Not done.	
G. R.	Surg. No. 24203	8	Tuberculous meningitis.	Yes. (partial).	0.	+. 5 wks.	Not done.	
C. T.	Med. No. 24277	8	Tuberculous meningitis.	Yes.	0.	+. 3 wks.	Not done.	
J. J.	H. L. H. Disp. No. 15178	1	Tuberculous meningitis. Pulmonary tuberculosis.	No.	0.	+. 6 wks.	+. 3 mos.	
E. C.	Med. No. 38345	41	Tuberculous meningitis. Pulmonary tuberculosis.	No.	0.	+. 6 wks.	Done. Guinea-pig died prematurely.	
H. L.	H. L. H. Disp. No. 14215	7 mos.	Miliary tuberculosis. Tuberculous meningitis.	Yes.	+.	+. 11 days.	Not done.	Guinea-pig inoculated with culture developed tuberculosis.
E. M.	H. L. H. Disp. No. 14950	8	Tuberculous meningitis. Miliary tuberculosis.	Yes.	0.	+. 10 days.	Not done.	Guinea-pig inoculated with culture developed tuberculosis. Blood culture +.
L. M.	H. L. H. Disp. No. 15068	4	Tuberculous meningitis. Miliary tuberculosis.	No.	+.	+. 7 days.	+. 3 wks.	Guinea-pig showed tuberculosis only in regional and iliac glands. Blood culture +.
R. A.	H. L. H. Disp. No. 2945	4	Tuberculous meningitis. Miliary tuberculosis (?).	No.	+.	+. 7 days.	+. 4 wks.	Guinea-pig showed tuberculosis only in regional and iliac glands.
W. G.	Med. No. 23453	5	Tuberculous meningitis.	No.	Not done.	0.	Not done.	
M. H.	Med. No. 23799	20	Tuberculous meningitis.	Yes.	0.	0.	Not done.	Blood culture 0.

JOINT FLUIDS.

J. C.	Surg. No. 23121	58	Tuberculous arthritis of knee. Pulmonary tuberculosis.	....	+.	+. 3 wks.	Guinea-pig died in 10 days without lesions.	Tissue at operation tuberculous
F. D.	Surg. No. 23960	20	Villous arthritis of knee.	No.	Not done.	+. 3 mos.	Not done.	
S. W.	Surg. No. 24214	47	Tuberculous arthritis of ankle.	No.	Not done.	0.	Not done.	

ABSCESS OF RIB.

L. C.	Surg. No. 23966	50	Tuberculosis of rib. Abscess of chest wall, tuberculous.	....	Not done.	+. 4 wks.	Not done.	Tissue tuberculous.

PERITONEAL FLUIDS.

W. W.	Med. No. 23717	35	Cirrhosis of liver. Chronic gastritis.	....	.....	0.	0.	Probably not tuberculous.

ABSCESS OF NECK.

J. L.	Surg. No. 24168	63	Abscess of neck, tuberculous. Healed tuberculosis of hip.	No.	Not done.	+. 6 wks.	Not done.	Abscess probably arising in sternoclavicular joint.

tory strains, or this may occur only after repeated transfers. In the first case, the sediment obtained after laking the blood, when spread over blood-agar slants, was so thick that growth did not become recognizable for 25 days. In order to obtain positive cultures in the shortest possible time (therefore making the method more useful as a diagnostic procedure), it may be desirable to reduce the bulk of the sediment still further by digestion with antiformin (as originally suggested by Uhlenhuth and Kersten for cultures from sputum and other tuberculous material) and inoculation of the washed sediment directly on blood agar. This method would also be of value if the blood had accidentally become contaminated, or in the case of autopsy blood cultures where post-mortem invasion of the blood by other organisms may have occurred. Blood cultures done by this method are in progress at the present time. It is also possible that the use of other media, such as Dorset's egg medium, or glycerine beef agar, might give positive results in a shorter period of time, and in a larger percentage of cases. Human-blood-agar was used in my cultures because it was easily available.

Negative blood cultures by one or another of these methods were obtained in two out of the seven cases of acute miliary tuberculosis studied. In one of these cases only 2 c. c. of blood were available for culture, and 1 c. c. for guinea-pig inoculation. The guinea-pig has remained healthy for five months, and has no enlargement of the inguinal glands.

Negative blood cultures were obtained in nine cases of other types of tuberculosis, and guinea-pig inoculations done in four of these cases were negative as well. Of these cases one was a tuberculous peritonitis; a second, an acute tuberculous broncho-pneumonia; a third, a chronic pulmonary tuberculosis in the second stage; a fourth, a pulmonary tuberculosis with adenitis and tabes mesenterica; and the remaining five, cases of tuberculous meningitis.

Cultures from the sediment obtained by centrifugalizing other tuberculous fluids have also been made by planting the sediment directly upon blood agar slants and sealing them. The results of these cultures, and of control smears and guinea-pig inoculations when made, are recorded in Table II.

In the work summarized in Table II no attempt was made to watch the cultures for the earliest date at which growth appeared, except in the last four positive spinal fluid cultures in the table, and parallel smears and guinea-pig inoculations were not done in every case. Of the 16 spinal fluid cultures two were negative and 14 were positive. In seven of the cases positive by culture, tubercle bacilli could not be demonstrated in smears. Four pleural fluids were cultured with one positive result. Smears from this positive case were negative, but a guinea-pig inoculated with the fluid developed generalized tuberculosis. The three negative cases were negative also by guinea-pig inoculation, and two of the three by smears as well. Tubercle bacilli were grown in culture from two out of three fluids from tuberculous joints, and from the pus from an abscess of a rib and an abscess of the sternum. One peritoneal fluid and one pericardial fluid were negative by culture and by guinea-pig inoculation. Both of these cases were probably not tuberculous.

Summary and Discussion.

In this work tubercle bacilli have been grown in culture for the first time from the circulating blood of five patients with miliary tuberculosis.

In the first method used the blood was added to glycerine-broth flasks, and after a preliminary incubation the sediment was planted on blood-agar slants, which were sealed and incubated. Three positive cultures were obtained by this method. In order to shorten the period of time necessary for growth to become visible, a second method was tried in which the blood was hemolyzed with distilled water and the centrifugalized sediment planted directly on blood agar slants. Three positive cultures were obtained from two patients by this method in 25, 13, and 7 days. In order to reduce still further the bulk of the sediment, and hence the period of time necessary for growth to become visible, a third method is suggested consisting in the digestion of the sediment by means of antiformin. Further work is being done with this method.

In order to be of value, cultural methods for the demonstration of tubercle bacilli in the blood must give positive results sooner and more constantly than the method of guinea-pig inoculation. The data at hand are insufficient to permit any definite conclusions, and further work is being done as cases are available, to determine these points. The experiment with the artificially seeded blood culture, and the three positive cultures obtained by the second method, indicate that growth may be obtained with appropriate methods in from one to three weeks. This is considerably under the time within which a positive result could usually be obtained by guinea-pig inoculation. The injection of blood subcutaneously into the groin of a guinea-pig produces an induration which will mask the development of a moderate glandular enlargement for several weeks, and prevent an early diagnosis of inoculation tuberculosis in this way. Furthermore, tuberculosis produced in guinea-pigs by the injection of blood containing tubercle bacilli may be very slow in developing, as claimed by Marmoreck in his work with experimentally infected guinea-pigs, and by others, using the blood of human cases. (Baetge, Rumpf and Zeissler.)

As regards the relative constancy with which results can be obtained by culture and by guinea-pig inoculation, nothing definite can yet be said. Under favorable cultural conditions, one might expect that one organism in the blood would produce a growth, while an appreciable number (varying inversely with the virulence) are needed to infect a guinea-pig. In the third case in my series half of the blood was injected into two guinea-pigs, neither of which became infected, while growth was obtained from the half cultured; and in the fourth case in which the blood culture was positive, the guinea-pig inoculated with one-fifth of the blood obtained died of intercurrent disease at the end of three months with no evidences of tuberculosis. Furthermore, guinea-pigs may die too soon for the development of macroscopic or microscopic lesions, either from the effects of the injection or from some intercurrent disease. This occurred in four of the control guinea-pig inoculations, one with blood, one with spinal fluid, one with joint fluid, and one with culture. The evidence at hand, then, would

indicate that suitable cultural methods will probably yield positive results more promptly and more regularly than animal inoculations.

The methods of demonstrating tubercle bacilli in the blood by means of smears have been shown to be unreliable, but when cultures are obtained from the blood we have conclusive evidence of the existence of a bacillemia.

On the other hand smears made from clear fluids with relatively little sediment frequently give reliable results by direct staining methods. In this series, however, tubercle bacilli were demonstrated more frequently by culture than by smears, as one would expect with favorable cultural conditions if the number of organisms is small. In the examination of one pleural fluid and seven spinal fluids for tubercle bacilli by smears and by culture, the smears were negative while the cultures were positive. In no instances were smears positive without the culture being positive also.

The practicability of blood cultures as a diagnostic method will depend upon the frequency with which the tubercle bacillus enters and persists in the blood stream. That bacillemia occurs frequently in miliary tuberculosis is shown by the high percentage (66.6 per cent) of positive results obtained by various authors in these cases by the method of guinea-pig inoculation with blood (Table I), and by the relatively large number of positive cultures obtained in the small series reported here (five out of seven cases). On the contrary this is probably a relatively uncommon phenomenon in pulmonary, and other forms of localized tuberculosis. Out of 1297 cases collected in Table I, only 6.7 per cent of guinea-pig inoculations with blood gave positive results, and in my series all of the blood cultures in these cases were negative.

In spite of the large amount of work which has been done on the subject of bacillemia in tuberculosis there is very little information which is based upon reliable methods of study. It has been shown definitely that tubercle bacilli may enter the blood stream, but relatively little is known as to the conditions in which bacillemia occurs, its frequency and regularity, the number of organisms present, or its diagnostic or prognostic significance.

The conditions in experimental tuberculosis in animals are somewhat better understood because the exact pathological lesions present can be determined, and to certain extent controlled. The bacillemia following the injection of tubercle bacilli has been studied by various investigators by the inoculation of guinea-pigs with blood from the infected animals. Some authors (for example Moewes) obtained positive inoculation tuberculosis by the injection of blood from experimentally infected animals in a large percentage of cases, while others in similar experiments obtained negative results (Sawyer). These divergent results are probably to be explained partly by differences in the virulence of the infecting organism, in its dosage and mode of administration, and in the time elapsing after inoculation before blood was withdrawn for the test. Marmoreck in 1907 published a detailed report upon this point. He found that after intravenous injection into guinea-pigs, the bacilli disappear from the blood after one to two days and recur four to six weeks later; after arterial inoculation they disappear after one to two days and recur 5 to 14 days later. After subcutaneous inoculation bacilli appear for the first time in the blood after 30 to 60 days, following inoculation into the anterior chamber of the eye, somewhat sooner; and still earlier (14 to 20 days) after intraperitoneal injection. The relation of the virulence of the bacilli injected to their persistence in the circulation was studied by Hess, who found that the feebly virulent strains persist less long in the circulation after inoculation, and reappear later than do virulent strains.

Tuberculosis, as it commonly occurs in man, is not exactly analogous to that produced experimentally in animals, and a similar study of the bacillemia in human tuberculosis would be desirable. Blood cultures repeated at frequent intervals, supplemented, perhaps, by guinea-pig inoculations, would seem to offer a favorable method for determining not only the existence of a bacteriemia, but, approximately at least, the number of organisms present.

Blood cultures, then, are suggested as an aid in the differential diagnosis of acute miliary tuberculosis from other, non-tuberculous, infections and as a means of studying bacillemia in all forms of tuberculous disease. Direct cultures from spinal, pleural, peritoneal, and other fluids are recommended in those cases in which tubercle bacilli cannot be demonstrated by smears.

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FIBROID TUMORS OF THE VULVA.

A REPORT OF 12 CASES AND A DIGEST OF THE LITERATURE ON THIS SUBJECT.

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Fibroid tumors of the vulva, although rather uncommon, are by far the most frequent of the benign, solid neoplasms found in this region. An idea of their frequency may be gathered from the fact that but six cases have appeared among 23,000 gynecological admissions to The Johns Hopkins Hospital.

The tumor usually appears first as a small, firm, painless nodule immediately beneath the skin of the labium majus. Its growth may be extraordinarily rapid, and the tumor usually soon becomes pedunculated. Growth continues and actual interference with locomotion may be the first inconvenience experienced by the patient.

When seen by the surgeon these tumors have in most cases developed a well-marked pedicle, and, hanging between the thighs, present a most remarkable picture. The upper surface of the tumor and the skin of the pedicle may be covered by hair. The skin covering the tumor is generally thick and thrown into numerous shallow folds and wrinkles at once suggesting the skin of the scrotum. The skin is freely movable over the tumor and its surface is usually quite unbroken. On palpation a firm, smooth or slightly lobulated mass is made out which is quite insensitive to moderate pressure. One or more pulsating vessels may be felt in the pedicle. On pulling the tumor and thereby making tension on the pedicle, a tough fibrous cord may sometimes be made out traversing the pedicle and entering the inguinal canal.

As the tumor grows the circulation may be impaired and the growth become œdematous and semi-fluctuant to palpation. The wrinkles and folds in the skin then disappear, the surface of the tumor becomes smooth and shiny and ulcerations commonly appear at the most dependent portion. In many cases the tumor undergoes just these changes during menstruation. The tumor may swell to twice its size during the menstrual period (Penrose [102]), become soft and quite sensitive and rapidly assume its former size, firm consistency and relative insensitiveness soon after the cessation of menstruation. Should pregnancy occur the tumor usually shows the same changes, but in addition may take on a very rapid growth.

The remarkable resemblance of some of these tumors, especially those of the labium majus, to the scrotum, has been commented upon frequently in the literature.

In at least one case (Coates [28]), a diagnosis of hermaphroditism was made, the firm, rounded elastic tumor being mistaken for a testicle.

Fibromata developing in the extraperitoneal portion of the round ligament have led to the most frequent mistakes in diagnosis.

A tumor appearing in this region has often been mistaken for an inguinal hernia (Heidemann,[66] Von Recklinghausen,[111] Verneuil,[122] etc.), and in some instances the patient has worn a truss until the increase in size demanded surgical intervention (Doormann [35]). This is perhaps not surprising, for a tumor in this region may appear very much like an inguinal hernia and may even be reducible through the inguinal canal (Nebesky [84]). In addition there may actually be a hernia in association with the tumor of the round ligament, as reported by Hecker,[61] Hofmorkel,[68] Landau,[76] etc.

Ordinarily fibroid tumors of the vulva cause no symptoms, other than the inconvenience dependent upon their size and weight and, if pedunculated, by their chafing and interference with locomotion. The tumor may become swollen and sensitive during menstruation and pregnancy and, if ulcerations follow the œdema usually associated with the increased vascularization under these circumstances, infection may render the tumor quite sensitive. The same sensitiveness may develop should the tumor undergo malignant change, a rather frequent outcome, in which event it usually ulcerates. Even the large sessile fibroids of the vulva rarely cause pain or pressure symptoms. Those developing in the rectovaginal septum may cause constipation, and in one case reported by Villiers and Damage [120] retention of urine was caused by the pressure of a calcified fibroid of the vestibule on the urethra. Itching has been mentioned occasionally as a prominent symptom (Ill [69]).

As the tumor increases in size it may render coitus practically impossible (Coates [27]), while interference with parturition has been reported by Albert.[1]

Etiology and Pathology.—With very rare exceptions fibroid tumors of the vulva occur within the child-bearing period. Esser,[41] Polaillon [105] and Weber [130] have each reported a case in which the tumor probably developed after the menopause, while Goldreich,[56] in 1909, presented a case of a pedunculated fibroma of the right labium in a nursing baby. That such exceptions are rare is probably due to the marked influence which menstruation and pregnancy exert on these tumors.

Fibroid tumors of the vulva grow more rapidly and attain greater size than superficial fibroid tumors in any other part of the body, while those originating in the subperitoneal areolar tissue and usually appearing first at the vulva are the real "giant" tumors of pathology, being the largest tumors known to the literature (Whitney and Harrington [128]).

That tumors of the vulva are subject to a marked periodic increase in blood supply in association with menstruation is plainly evident from the changes, such as swelling and tenderness, which have often been noted during the period.

Again, during pregnancy they are subject to a prolonged increase in blood supply and in consequence usually take on a very rapid growth.

These tumors may develop from the connective tissue of almost any of the vulval structures, such as the subcutaneous connective tissue of the labium majus or labium minus. They may likewise take their origin in the extraperitoneal portion of the round ligament or in some pelvic structure such as the subperitoneal areolar tissue, and growing in the direction of least resistance may appear at the vulva in the region of the labium majus, perineum or buttock.

Fibroid tumors of the vulva are more prone to degenerative processes than similar tumors in any other part of the body. This is due to two factors. These tumors are subjected to marked variations in their blood supply during menstruation and pregnancy, which cause a rapid growth. Growing rapidly, the majority soon become pedunculated, that is, they develop ideal mechanical conditions for degenerative processes. Œdema, lymphangiectases, hyaline and cystic degeneration, calcification, ulceration and infection as well as gangrene and both myxomatons and sarcomatons metamorphoses, have all been reported in the literature.

Before discussing the histogenesis and mode of growth of these tumors I shall report briefly the cases which have appeared in this clinic, and the specimens which have been sent to the laboratory of gynecological pathology.

Case I.—Gyn. No. 21735. I. F., aged 17, colored.

Clinical History.—The family and personal histories were unimportant. The patient had never been pregnant. Menstruation began at the age of 15 and continued normally.

Present Illness.—About one year before admission the patient noticed a very small firm swelling just to the right of the vaginal orifice. It had been growing rapidly ever since. It itched occasionally but otherwise there was "no feeling in it." At times the tumor would swell slightly. The only discomfort was caused by its size and weight, and its interference with locomotion.

Examination (Fig. 1).—Springing from the lower portion of the right labium majus is a large pear-shaped pedunculated tumor measuring 19 cm. in length. The tumor part is quite distinct from the pedicle and is 14 cm. in length by 9.8 cm. in its greatest diameter. The pedicle measures 4.8 cm. in length and 1.3 cm. in diameter at the tumor and 2.3 cm. at the base. The surface of the tumor is covered with normal-looking skin except at the lower extremity, where there is a small ulceration 1 cm. in diameter. The surface temperature is normal.

The tumor is soft and feels somewhat lobulated. There is no superficial sensation on pinching or tapping the surface. On squeezing the whole mass between the hands, the patient complains of discomfort. There are several crypt-like depressions in the skin over the upper part of the tumor, measuring 1 or 2 mm. in depth.

The pedicle contains no palpable vessels. There is no hair on the surface of the tumor, but there is a small amount scattered over the base of the pedicle. No cord-like structure can be felt in the pedicle, and traction on it shows that there is no connection with the round ligament or with any structure in the upper portion of the labium or the canal of Nuck.

Operation.—Simple amputation at the vulva by an oval incision 2 x 3 cm. about the base of the pedicle. No large vessels encountered. Convalescence uneventful. Healing per primam.

Pathological Description.—On section, a soft, pearly white, somewhat translucent surface is presented from which a quantity of clear limpid fluid exudes on slight pressure. Three small cystic cavities are seen, containing the same clear fluid. The largest of these measures 9 mm. in diameter, and is limited by a definitely calcified wall. Here and there rather large vessels are seen, the walls of which are thickened and for the most part partially calcified. In one place a completely calcified vessel is seen, and can be traced about an inch.

Scattered over the surface are numerous, very small cystic spaces containing clear fluid, and giving certain areas of the cut surface a spongy appearance. The cut surface of the pedicle shows a few blood-vessels, but no fibrous cord.

Microscopic Examination.—The skin covering the tumor is quite normal. Near the pedicle normal skin elements, such as hair follicles and sweat glands, are seen. These are not present in the skin over the rest of the tumor.

The body of the tumor is quite cellular and is made up of connective-tissue cells arranged in loose strands running in all directions. In places the cells are widely separated. The cytoplasm is spindle-shaped or branching. The nuclei are round, oval or spindle-shaped and are vesicular. There are extensive areas of hyaline degeneration throughout the tumor.

The larger cystic spaces are lined with a single layer of endothelium and their thickened fibrous walls are undergoing calcification.

The smaller spaces seen in the spongy areas described above, are dilated lymphatics and are very numerous. They are lined with a single layer of endothelium.

The blood-vessels are fairly numerous. There is a scant round-cell infiltration about a few of the smaller vessels. The walls of the larger vessels are thickened and some are becoming calcified.

In one area a very small group of smooth muscle fibers is found.

The pedicle is made up of rather dense bundles of connective tissue and a few bands of smooth muscle, both showing marked hyaline degeneration. A number of large blood-vessels are seen, some of which appear quite normal, others showing thickened walls, hyaline degeneration and calcification.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated, with lymphangiectases, extensive hyaline degeneration and beginning calcification.

Case II. Gyn. No. 10670. V. T., aged 40, colored.

Clinical History.—The family and personal histories were of no importance. She had had one child 23 years before admission to the hospital. After a normal menstrual life the menopause had appeared three years before with typical symptoms.

Present Illness.—Eight years before admission a small red itching nodule appeared on the left labium majus. For six years it grew very slowly but quite steadily. During the two years before admission the tumor rapidly increased in size.

During the menstrual periods the tumor had usually become swollen and sensitive. Since the complete cessation of menstruation the tumor had continued to show periodical monthly changes. At the same time each month the tumor would become greatly swollen and very sensitive. At the end of four or five days the swelling and sensitiveness would disappear, the tumor resuming its usual shape and size. Otherwise there had been no discomfort except rather marked interference with locomotion.

Examination.—Suspended from the left labium majus is a pear-shaped pedunculated tumor covered with normal skin. In appearance the tumor is very similar to that seen in Case I (Fig. 1), except that it is somewhat larger and is attached to the left instead of the right labium majus. There are no ulcerated areas. From the base of the pedicle the tumor measures 22 cm. The pedicle is 7 cm. long and 2 cm. wide; the tumor is 15 cm. long and 8.5 cm. in its greatest diameter.

On palpation the tumor is found to be rather soft and is not lobulated; no cord-like structure can be made out in the pedicle. No sensation is caused by squeezing the tumor.

Operation.—Under local anæsthesia (Schleich), the tumor was removed by an elliptical incision about the base of the pedicle. Closure with silk. Healing per primam.

Pathological Description.—The surface of the tumor is covered with normal skin which is thrown into numerous shallow folds giving it the appearance of a scrotum. There are no ulcerations. A few large hair follicles are visible in the region of the pedicle.

On section a smooth white glistening translucent surface presents which is homogeneous throughout. On pressure a small quantity of clear fluid exudes from the cut surface. There are no areas of softening or cystic change.

Microscopic Examination.—The tumor is composed of pure fibrous tissue, the bundles of fibers showing a marked tendency to arrange themselves in parallel strands. The strands of fibers are loosely arranged and in places the tissue is seen to be definitely œdematous. There is extensive hyaline degeneration throughout. Everywhere the tissue is poor in cells. What nuclei there are, are oval or spindle-shaped, quite pale and vesicular. The blood-vessels are of moderate size and number. The smaller vessels are for the most part surrounded by limited but dense round-cell infiltrations. Next one of the larger vessels is a clump of fat cells. Beneath the normal skin which covers the tumor there is a slight round-cell infiltration. No smooth muscle fibers are seen in the body of the tumor.

The pedicle contains a number of large blood-vessels and a few strands of smooth muscle; the skin in this region contains a number of hair follicles.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated, with œdema and extensive hyaline degeneration.

CASE III. Gyn. No. 8518. E. H., aged 22, white.

Clinical History.—The family and personal histories were unimportant. The patient was single. She began to menstruate at 14. The periods were somewhat irregular at times, the interval varying from 3 to 5 weeks. The flow had always been scant, of 4 or 5 days' duration and attended with considerable pain.

Present Illness.—Six years before admission to the hospital the patient noticed a lump in the lower portion of the left labium majus, about the size of the "last joint of the thumb." For four years the growth was steady but slow. During the two years before admission to the hospital the tumor rapidly increased in size. There had been no discomfort except the inconvenience to locomotion and occasional chafing. No changes in the tumor had been noted during menstruation, and it had remained of about the same consistency from the first.

Examination (Fig. 2).—The left labium majus forms the base of a large pedunculated tumor. The pedicle occupies the entire labium. From a point opposite the clitoris the tumor measures 16 cm. in length. From a point opposite the fourchette (lower portion of the base of the pedicle) it measures 11 cm. in length. The tumor itself is 7 cm. in diameter at its widest point. On palpation the mass is made out to be definitely lobulated and rather soft. It is covered with normal skin, which in the region of the pedicle and about the base of the tumor is covered with normal labial hairs. The pedicle contains some large pulsating vessels.

Operation.—The tumor was removed by an elliptical incision about the base of the pedicle. Convalescence uneventful. Healing per primam.

Pathological Description.—The specimen consists of a rather soft nodular tumor covered with normal skin which is thrown into numerous folds giving it the appearance of a scrotum, an appearance which is accentuated by a number of rather large blood-vessels which can be seen just beneath the skin surface. The skin is but loosely attached to the underlying mass.

On section the bulk of the tumor is seen to be made up of a rather firm mass measuring 7 cm. in diameter. The cut surface is smooth, homogeneous, pearly white, glistening and translucent, and on pressure a small amount of clear fluid exudes. Surrounding this main nodule are 15 or 20 smaller but similar ones. These vary from a few millimeters to 2.5 cm. in diameter and all show the same characteristics on section.

Microscopic Examination.—The tumor is composed of fibrous tissue arranged in rather loose strands running in all directions, but here and there showing a definite tendency to become parallel. The entire tumor is quite cellular, the nuclei being large and vesicular and oval or spindle-shaped. Everywhere there is extensive hyaline degeneration. A very few large fat cells are scattered sparsely throughout the tumor tissue, there being usually not more than two or three in a single field and large areas of tissue completely devoid of any adipose elements. The blood-vessels are quite numerous and of moderate size. About some of them there is a moderate round-cell infiltration. No œdema. No smooth muscle.

Diagnosis.—Fibroma, labium majus, pedunculated, with hyaline degeneration and slight adipose infiltration.

CASE IV. Gyn. No. 3896. M. T., aged 32, white.

Clinical History.—The family and personal histories were unimportant. The patient had been married 11 years before admission to the hospital and had had one child. Menstruation became established at the age of 16 and had always been regular and normal except for rather severe pain on the first day.

Present Illness.—The patient first noticed a small hard lump in the left labium majus 18 months before admission. It was not sensitive. For a year it grew slowly, but for the six months preceding admission had taken on a very rapid growth. For three months it had been ulcerated and quite painful.

Examination (Fig. 3).—The vaginal orifice is occluded by a large semi-fluctuant tumor in the base of the left labium majus. The tumor is reddened, sensitive, and on its vaginal surface presents an ulcerated area from which blood is oozing. The tumor occupies the region of Bartholin's gland, is well circumscribed and does not infiltrate the tissues above or below. There is no enlargement of the inguinal glands.

Operation.—The tumor was excised with a wide area of skin about it and a considerable amount of the underlying areolar. The patient left the hospital in 12 days, the wound being healed except for a minute granulating area at the lower angle.

Pathological Description.—The specimen consists of a tumor nearly spherical in shape and measuring 5.5 x 4.5 cm.

One half of its free surface is covered with normal skin, the other half with vaginal mucous membrane. Springing from the vaginal surface near the muco-cutaneous border is a mass 3 x 2.5 cm. and projecting 1 cm. above the level of the mucosa. One half of this mass is smooth, the other half ulcerated and deeply excavated.

On section a striking picture is seen. Surrounding the entire tumor, with exception of the base of the mass projecting from the vaginal surface, is a narrow capsule of firm tissue composed of parallel fibers.

The central portion of the tumor, which measures 3.7 cm. in diameter, is sharply differentiated from the surrounding tissue. It is of a much lighter hue and is composed of a loosely arranged fibrillated meshwork, crossed by a few fine bands of somewhat denser and darker tissue.

Beneath the vaginal surface the capsule on section presents a crescentic surface extending from the ulcerated area at the muco-cutaneous border to the opposite pole of the tumor. Here the capsule has been split and separated into two layers by the invasion of tissue of a darker color than the other portions of the tumor. This layer of tissue is continuous with the ulcerated area

on the surface of the tumor, being composed of roughly parallel, loosely arranged fibers which, converging toward the ulcerated mass, radiate out to form it. This layer contains a few islands of very pale tissue, the largest of which measures 5 x 3 mm., similar to that composing the central portion of the growth.

Microscopic Examination.—With the exception of the nodule projecting from the surface, the tumor is surrounded by a distinct capsule, the free surface of which is covered by stratified squamous epithelium. The capsule is composed of parallel layers of connective tissue, which show marked hyaline degeneration. Just beneath the epithelium there is a moderate round-cell infiltration. Toward the skin surface bundles of non-striped muscle fibers, hair follicles, and other skin elements are present.

At the base of the nodule, at the muco-cutaneous border, the connective-tissue layer entirely ceases, but the epithelium continues a short distance over the sides of the nodule, the tumor then presenting a granulating surface.

The central portion of the tumor is composed of a meshwork of large spindle-shaped fibers, having spindle-shaped, or occasionally oval, vesicular nuclei. The greater portion of the tissue is rarefied, the cells very large and separated by a delicate blue-tinted substance. Running across the tissue in various directions are bands of denser formation containing blood-vessels of considerable size. The nuclei of these cells are, for the most part, spindle-shaped and vesicular, and about the size of the nuclei of smooth muscle fibers. There is, however, a considerable variation. Many of them are large, being three or four times the size of the others, oval and vesicular, and here and there are scattered cells containing exceedingly large, deeply staining nuclei, frequently vacuolated. Frequent irregular mitotic figures are found. Throughout the tissue there is a moderate round-cell infiltration, and in the looser portions are seen a number of mast cells. There is a fair vascular supply, the vessels being very thin-walled. The crescentic band of tissue running from the ulcerated portion to the opposite pole of the tumor is essentially the same as that just described, but here the fibers are densely packed. Scattered through it here and there are myxomatous areas of varying size.

At the base of the ulcerated nodule the cells become very abundant, and continuing directly into it form radiating strands to the surface. The nodule is very cellular and has a rich supply of blood-vessels, the surface being formed of capillary loops covered over with a dense layer of leucocytes.

Pathological Diagnosis.—Fibromyxosarcoma, labium majus.

Case V. Gyn. No. 15229. M. A., aged 45, white.

Clinical History.—The family and personal histories were unimportant. She had been married 21 years and had borne nine children, the youngest of whom was 14. Menstruation began at 12 and had continued regular and normal up to the age of 42, since when the periods had become irregular.

Present Illness.—For several years the patient had noticed some small tumors near the vaginal orifice, which had gradually increased in size. They had never given any symptoms.

Examination.—Hanging from the left labium majus by a short pedicle measuring 5 mm. in diameter is a tumor measuring 7.5 cm. in length and from 5 to 6.5 cm. in diameter. The tumor is insensitive, is covered with normal skin and is dark purplish in color.

On the inner surface of the right labium majus there are two small but thick-walled cysts, one of which is open and infected.

There is a marked anterior relaxation with a large cystocele. The cervix is greatly hypertrophied. The uterus is of normal size and is in good position. The adnexa are normal.

Operation.—The tumor of the left labium was removed by an incision about the base of the pedicle. The two cysts in the right labium were then dissected out. Closure with catgut. Amputation of the cervix and anterior colporrhaphy were then completed.

Pathological Diagnosis.—Fibroma, labium majus. Pedunculated. Sebaceous cysts (two), labium majus. The specimen has been lost. No pathological description, therefore, can be given.

Case VI. Gyn. No. 13733. A. C., aged 35, white.

Clinical History.—This patient, who had had three children, was admitted to the hospital for the treatment of a severe chronic endocervicitis. The cervix was cauterized and a small firm nodule measuring 1 cm. in diameter, which she had never noticed, was removed from the left labium majus. The tumor was embedded in the tissue of the labium.

Pathological Diagnosis.—Fibroma, labium majus.

Case VII. Path. No. 22063. The abstract of the clinical history was kindly given us by Dr. Hunner, with whose permission this case is reported.

Clinical History.—The patient, a white woman, aged 47, a multipara, came to his office complaining of a small growth. She had had it for some time, but recently it had been getting sore and discharging pus, and for the past month had been bleeding at times.

Examination.—Showed a tumor of the left labium minus.

Operation.—After injecting the base of the pedicle with 1 per cent cocaine, the tumor was cut off with the Paquelin cautery and two pumping vessels controlled by dull heat.

Pathological Description.—The specimen consists of a small tumor removed from the left labium minus. Attached to a pedicle 13 mm. long and 8 mm. in diameter is a small, firm polypoid mass measuring 2.5 x 2 x 1.2 cm. The tumor is divided into two distinct lobules by a furrow 1 cm. deep. The entire surface is covered with thick, wrinkled skin and issuing from the depths of some of these wrinkles are a number of long hairs. There is a small ulcerated surface at the most dependent portion of the tumor.

On section, the cut surface near the pedicle is seen to be composed of very densely packed parallel strands of fibers which radiate out to form the tumor mass, which is composed of more or less loosely arranged fiber bundles running in various directions. In the central portion of the tumor these strands of tissue are separated by very numerous blood-vessels of considerable size, giving the surface a spongy appearance. The skin is seen to be distinctly thickened.

Microscopic Examination.—The very irregular surface is covered with a thick layer of normal squamous epithelium continuous over the entire tumor except at the ulcerated portion at the tip. Here there is a granulating surface thickly covered and infiltrated with leucocytes. The body of the tumor is made up of rather loosely arranged bundles of fibrous tissue widely separated in certain areas by numerous blood-vessels of considerable size. Throughout the entire tumor the fibrous strands show marked hyaline degeneration. The nuclei are abundant, and are for the most part spindled-shaped, but many large oval, vesicular forms are seen. Large areas throughout the tumor are heavily infiltrated with leucocytes and round cells.

Pathological Diagnosis.—Fibroma, labium minus, infected.

I wish to report briefly on the following specimens. In these cases no clinical history was obtainable, the specimens merely having been sent to the laboratory for diagnosis.

Case VIII. Path. No. 4056. The specimen consists of a large multinodular tumor removed from the labium majus. The mass is composed of a large number of small, firm, round tumors varying in size from a pea to 4 cm. in diameter and surrounded by a small amount of adipose and connective tissue.

Microscopic Examination.—The different nodules are all of essentially the same structure. Each is surrounded by a definite capsule of parallel bands of dense fibrous tissue. The stroma is composed of loosely arranged connective-tissue cells, large and

spindle-shaped or fusiform, and containing large oval or spindle-shaped vesicular nuclei. In a few places there is a slight tendency to strand formation, but for the most part no such tendency is suggested. Here and there areas rich in cells alternate with masses of hyaline tissue containing practically no nuclei. The nuclei are for the most part pale and vesicular, but here and there a number of very deeply staining nuclei are seen with finely granular chromatin. A number of large pale cells with very large, rather deeply staining vesicular nuclei are seen. The tumor is for the most part definitely œdematous.

Pathological Diagnosis.—Fibroma, multinodular, labium majus, œdematous, with hyaline degeneration.

CASE IX. Path. No. 2682. The specimen consists of a round polypoid growth removed from the labium majus and measuring 1.5 cm. in diameter. The surface is covered with thick, wrinkled skin. There is a short pedicle about 4 or 5 mm. in length. The tumor has a firm consistency.

Microscopic Examination.—The surface of the tumor is irregular, consisting of small finger-like papillæ covered with normal squamous epithelium. The cells of the deepest layer contain a golden brown, granular pigment.

The stroma is composed of fibrous tissue somewhat poor in cellular elements and containing a moderate amount of elastic fibers. There is no smooth muscle.

The cells, which are fairly evenly distributed throughout the tissue are long, spindle-shaped or branching, and contain large oval or elongated vesicular nuclei. Blood-vessels are fairly numerous and are of moderate size.

The superficial portions of the stroma show a slight round-cell infiltration.

Pathological Diagnosis.—Fibroma, labium majus, pedunculated.

CASE X. Path. No. 3033. The specimen consists of a small nodule measuring 7 mm. in diameter, removed from the inner surface of the labium majus to which it was attached by a very short pedicle.

Microscopic Examination.—The surface is covered with normal squamous epithelium, which presents somewhat marked papillary elevations. The tumor itself is composed of a fibrous stroma, fairly rich in cells. These are oval, fusiform or branching and contain large oval or spindle-shaped vesicular nuclei. There are a few round cells scattered sparingly between the tumor cells. A few large round cells with faintly straining cytoplasm and densely stained nuclei are seen. The blood-vessels are small and moderate in number. There are no muscle cells.

Diagnosis. Fibroma, labium majus. Pedunculated.

CASE XI. Path. No. 2027. The specimen consists of three small calcareous nodules removed from the labium majus and measuring 5, 8 and 10 mm. in diameter. One was decalcified and sectioned.

Pathological Diagnosis.—Calcareous nodules from labium majus, probably calcified fibromata.

CASE XII. Path. No. 5513. This specimen was received from the Frauenklinik, Strassburg. It consists of a small cuboidal piece of tissue removed from a tumor of the right labium majus. The gross specimen was ovoid, somewhat larger than an egg and perfectly encapsulated. It had the consistency of a fatty tumor. On section, the cut surface bulged and was somewhat mottled, the whole having much the appearance of a testicle.

Microscopic Examination.—The tissue is quite homogeneous, consisting of fibrillated tissue quite rich in cellular elements. The cells are more or less spindle-shaped and have vesicular nuclei of various sizes. The nuclei differ greatly in the intensity with which they take the stain. Mitotic figures, for the most part irregular, occur in small numbers. The blood-vessels are fairly numerous.

Pathological Diagnosis.—Spindle-cell sarcoma, labium majus.

HISTOGENESIS AND MODE OF GROWTH.

Despite the fact that almost every possibility finds an illustrative case in the literature, there are certain very definite points of predilection from which the majority of fibroid tumors of the vulva develop. I have arranged these below in what appears to be their order of frequency.

GROUP I. *Fibroid Tumors Originating in the Subcutaneous Connective Tissue; 70 cases:*
- (a) of the labium majus; 53 cases.
- (b) of the labium minus; 11 cases.
- (c) of the vestibule and vagina; 5 cases.
- (d) of the perineum; 1 case.

GROUP II. *Fibroid Tumors Originating in the Extraperitoneal Portion of the Round Ligament; 39 cases:*
- (a) and growing outward into the labium majus; 25 cases.
- (b) and remaining in the inguinal canal; 11 cases.
- (c) and growing back into the abdomen; 2 cases.
- (d) and growing up between the layers of the abdominal wall; 1 case.

GROUP III. *Fibroid Tumors Originating in the Subperitoneal Connective Tissue and Appearing at the Vulva; 1½ cases.*

GROUP IV. *Fibroid Tumors Originating in the Connective Tissue of Bartholin's Gland; ½ cases.*

GROUP V. *Fibroid Tumors Originating in Hæmatomata; 2 cases.*

GROUP VI. *Fibroid Tumors Originating in the Connective Tissue of the Rectovaginal Septum; 2 cases.*

GROUP I. FIBROID TUMORS ORIGINATING IN THE SUBCUTANEOUS CONNECTIVE TISSUE.

Fibroid tumors originating in the subcutaneous tissue of the vulva (Klob[73]) include more than half of the cases in the literature. As will be seen, the vast majority appear in the labia and soon become pedunculated. Likewise, a considerable majority of the tumors of long standing show some form of degenerative change. In this connection a point of considerable importance is brought out by the analysis. Of the 64 cases of fibroid tumors of the labia majora and labia minora reported, 14 cases, *or 22 per cent, showed a malignant (sarcomatous) metamorphosis.* In one case (Weber[140]) the sarcomatous change was definitely traced back to trauma.

In addition to the labia as a point of origin, rare instances have occurred in which the tumor has originated in the connective tissue of the vestibule (Churchill,[26] Parsons[109] and Thomas[122]); of the vagina (Elisher and Hasenbalg), and of the perineum (Newman[78]).

The following cases have been reported:

A. ORIGIN IN THE SUBCUTANEOUS TISSUE OF THE LABIUM MAJUS.

Albert.[1] A primipara, aged 25, nine months pregnant, showing a huge fibroma hanging from the left labium majus down to the knees.

Arcangelis.[4] Para-II, aged 48, had noted a growth the size of a pea in the left labium majus three years before. When seen, a tumor the size of a seven months' fœtal head was found hanging from the left labium by a pedicle 5 cm. long. Microscopic diagnosis, fibromyxosarcoma.

Bullard.[20] Para-II, aged 38, had found a small lump in the left side of the vulva two years previously. At present, a bag-like mass,

2 inches in diameter, is attached to the lower end of the left labium majus by a pedicle ½ inch in diameter. Microscopic diagnosis, fibroma. The center of the tumor is composed of loosely meshed connective tissue, while that at the periphery is dense.

Burr.[23] Para-IV, aged 42, had noticed a growth in the upper third of the left labium majus 18 years before. At the end of six years it had grown to the size of a walnut and was removed. Six years later the patient noticed a similar growth lower down in the labium majus, and later two more nodules appeared at the site of the first operation. The three tumors were removed and proved to be fibromata. Three years later there had been no recurrence.

Calmann.[28] A primipara, aged 22, in the fourth month of pregnancy, had had a small hard lump in the right labium majus, the size of a pea, since childhood. It had grown very slowly up to the time she had become pregnant, when it took on a rapid growth. On examination a tumor the size of an apple was found suspended from the middle of the right labium by a pedicle 10 cm. long and as thick as the little finger. Microscopic diagnosis, œdematous fibroma.

Canuyt et Princetau.[34] A woman, aged 29, had noticed a small tumor of the left labium majus one year before. A pedunculated tumor the size of a banana was removed, which proved to be a very vascular fibroma.

Eichholz.[39] A nullipara, aged 30, with a tumor of the left labium majus, 11 cm. long by 6 cm. broad. It had developed slowly from a small tumor first noticed at the age of three years. On removal, it was found to be a cavernous fibroma.

Esser.[41] Case (a). A nullipara, aged 35, had noticed a hard lump the size of a bean in the right labium majus four years previously. Examination showed a tumor the size of a child's head attached to the labium by a pedicle 9 cm. long. There was an ulceration on the inner surface. The patient stated that during menstruation the tumor became swollen and painful. Microscopically, the tumor proved to be an œdematous fibroma.

Esser.[41] Case (b). A woman, aged 51, with a tumor of two years' duration, found to arise from the left labium majus by a pedicle 3 cm. long. The tumor was about the size of a small pear. Microscopic diagnosis, fibroma.

Fürst.[47] Case (a). Para-II, aged 41, had noted a small wart-like prominence in the right labium majus 12 years previously. The tumor had grown steadily and would become swollen during menstruation. Examination showed a growth 13.5 cm. in circumference attached to the labium by a pedicle 8 cm. long by 1.5 cm. in thickness. Microscopic diagnosis, œdematous fibroma.

Fürst.[47] Case (b). Para-XI, aged 38, with a slow-growing tumor of the left labium majus the size of a duck's egg. Microscopic examination proved it to be a partly gangrenous spindle-cell sarcoma.

Gangolphe.[49] Para-V, aged 36, was found to have a fibromyoma embedded in the left labium majus. The patient stated that it would become swollen and sensitive during menstruation.

Garrigue[50] removed a pear-shaped, pedunculated tumor from the left labium majus, which measured 8 by 7 by 4 cm. The pedicle was as thick as a finger. The tumor had begun to slough and emit a foul odor. Microscopic diagnosis, œdematous fibroma.

Giles.[55] Primipara, aged 22, six months pregnant, came complaining of a tumor which had appeared a few months before. Examination showed a tumor the size and shape of a fresh fig attached to the lower portion of the left labium majus by a long thin pedicle. On removal, "it presented all the characteristics of a molluscum fibrosum." Giles considered that this growth had originated during pregnancy.

Graefe.[57] Para-III, aged 36, was found to have a tumor of the left labium majus, the size of a man's fist, attached by a short pedicle as thick as the little finger. The tumor had been present five years but had taken on a rapid painful growth during the past year. Microscopic diagnosis, fibroma, undergoing myxomatous change.

Grime.[59] Para-I, aged 41, showed an enormous pedunculated tumor of the right labium majus. It had been present for seven years and had begun to slough. The mass consisted of a number of tumors, the largest of which measured 25 inches in circumference, the next largest, 18 inches, and the third, 11 inches. A large number of smaller tumors varied in size from 3 by 2 inches to 1½ by 1 inch. The tumors were composed of hard fibrous tissue. The pedicle contained a large pulsating vessel. Weight 16½ pounds.

Handfield-Jones[61] operated on a woman, aged 28, who had a pedunculated tumor of the left labium majus, the size of a large fœtal head, at term. It had been present five years and had recently become ulcerated. Its growth had been gradual. Microscopic examination showed it to be a "pure myxoma."

Holzmann[67] removed a pedunculated fibroma weighing 6850 gm. from the right labium majus of a woman, aged 37. The tumor hung to the knees. Diagnosis, fibroma.

Ill[68] describes a case in which he removed a number of small papillomatous growths from the vulva of a patient, aged 58. The tumors were scattered over the labia majora and vestibule, were of one year's duration and had caused no symptoms other than itching. Microscopically, the tumors proved to be papillomatous fibromata.

Kayser[70] demonstrated a fibromyoma of the labium majus. The patient, aged 56, had passed the menopause two years previously. Although of only four years' duration, the tumor measured 34 cm. in circumference.

McClintock.[73] A multipara, aged 40, with a tumor of the right labium majus, stated that it had been present for 15 years. The growth hung from the labium by a pedicle as thick as three fingers. It was about the size of an orange, ulcerated, and was found to be composed of fibrous tissue.

McDonald[75] removed a myxoma of the right labium majus, which recurred during a subsequent pregnancy.

Marcano[85] operated on a woman, aged 25, who had had a tumor of the left labium majus for four years. At operation, the tumor was found to be very vascular and to extend into the recto-vaginal septum. It was about the size of an orange. Microscopic diagnosis, fibromyoma.

Michon[89] removed a hard, lobulated tumor from the right labium majus of a patient, aged 32. Microscopic diagnosis, fibroma.

Mond[90] saw a patient with a tumor of the right labium majus the size of a child's head. Although of seven years' duration it had given no discomfort, the patient applying for treatment because she was about to marry. At operation the tumor was found to be extremely vascular. Microscopic diagnosis, fibromyoma.

Monod.[91] Para-III, aged 30, had noted a nut-sized tumor in the left labium majus during her last pregnancy, six years previously. A sessile tumor was removed, which weighed 570 gm. and proved, on microscopic examination, to be a fibromyoma.

Morestin.[92] Case (b). A woman, 71 years old, came to operation with a fibroma of the left labium majus of 10 years' duration. The tumor was as large as two fists and hung by a pedicle down to the knees.

Odelbrecht[96] removed a hard tumor from the right labium majus of a woman 40 years of age. The tumor was larger than a man's fist and had developed in 10 months. At operation it was found to be embedded in the labium and reached up to the clitoris and down to the anus. It extended upward along the vagina halfway to the cervix. Microscopic diagnosis, fibroma.

Oreillard.[97] A patient, aged 27, complained of a tumor of the left labium majus of seven years' duration. The tumor had at first been sessile but had become pedunculated. Examination showed

a tumor 22 cm. in circumference, ulcerated on its inner surface and hanging by a pedicle 10 cm. long. Microscopic examination showed it to be a very vascular fibromyxoma.

Orloff [98] removed a spindle-cell sarcoma of two years' duration from the labium majus of a patient, aged 30. It weighed 100 gm.

Penrose.[102] Six months after her delivery at term, eight years before, a patient, aged 41, para-II, noticed a small hard lump in the right labium majus, which had been growing steadily since. Examination showed a pear-shaped tumor the size of a fist hanging from the labium by a pedicle 10 inches long. The pedicle contained a pulsating artery the size of the radial and the patient stated that during menstruation the tumor would swell to twice its size. Microscopic examination showed a very vascular, œdematous fibroma, undergoing myxomatous changes.

Perewaloff [103] describes a 31-pound fibroma of the labium majus of seven years' duration. It hung to the knees.

Ponzian.[106] A patient, aged 35, para-VIII, had noticed a small tumor in the right labium majus 12 years before. Examination showed an ulcerated tumor the size of a pear hanging by a pedicle 5 cm. long. Microscopic diagnosis, fibroma.

Ritchie [113] removed a small pedunculated tumor from the labium majus, which proved, on microscopic examination, to be a fibroma.

Rosenthal.[114] A patient, aged 53, had noticed a small wart-like nodule on the right labium majus for a number of years. Six months previously it had taken on a rapid growth. Examination showed an ulcerated tumor the size of an apple hanging by a pedicle 4 cm. long and as thick as the little finger. Microscopic diagnosis, fibromyoma, showing recent myxomatous change.

Scanzoni [115] removed a pedunculated fibroma the size of a man's fist, which hung from the right labium majus to the middle of the thigh. Aside from the swelling and sensitiveness during menstruation, the tumor had caused no symptoms.

Schiele.[119] A patient, 26 years of age, had had a hard painless swelling in the left labium majus for 11 years. On examination a tumor the size of a child's head was found suspended from the lower portion of the left labium by a pedicle 2.7 cm. long. On section, two cystic cavities the size of an olive were found. Microscopic diagnosis, œdematous fibroma.

Schumann.[121] Para-VI, aged 45, had noticed a small hard lump in the left labium majus for eight years. Its growth had been slow but steady. Examination revealed an ulcerated tumor the size and shape of a pear hanging from the labium by a pedicle 10 cm. long and 2 cm. in thickness. Microscopic diagnosis, myxomatous fibroma.

Schwaiblmair [122] describes a case in a woman 29 years of age, who developed in the course of four years a tumor of the left labium majus weighing 1740 gm. Microscopic diagnosis, myxofibroma.

Selcke [125] operated on a nullipara, aged 20, who had had a tumor of the left labium majus for three years. During the past year it had become pedunculated. The tumor measured 15 cm. in length and the pedicle, 4 cm. Microscopically it was composed entirely of fibrous tissue and showed a number of greatly dilated lymph spaces.

Simpson-Barbour.[126] Case (b). A virgin, aged 16, had noticed a swelling the size of a plum three years previously, in the right labium majus. The tumor was at first sessile but soon became pedunculated. It was ulcerated and had been bleeding, and had grown to the size of a large fist. Microscopic diagnosis, fibromyxoma.

Souligoux [129] removed a fibrolipoma, the size of an orange and of 14 years' duration, from the right labium majus.

Strina [128] operated on a patient, aged 24, showing a pear-shaped tumor measuring 7 by 4 cm. and hanging from the right labium majus by a pedicle 10 cm. long. A microscopic section proved it to be a fibromyoma in the initial stages of degeneration.

Szili [130] removed a tumor the size of a goose egg from the right labium majus of a patient, aged 37, para-IV, which had been present for four years. Microscopic diagnosis, spindle-cell fibrosarcoma, containing a number of giant cells.

Tarnier [131] describes a case in which a large fibroma of the labium majus increased rapidly in size during pregnancy and after labor returned to its former dimensions.

von Tischendorf.[133] A virgin, aged 22, had noticed a tumor of the left labium majus seven years previously, which had grown steadily to the size of a fist and had become pedunculated. Microscopic examination showed it to be an œdematous fibroma. In places the skin epithelium showed rapidly proliferating basilar processes penetrating far downward.

Tuttle [134] operated on a woman, aged 52, para-III, who had noticed a painless lump in the right labium majus four years previously. It had grown steadily and had doubled in size in the last year. The only symptoms were from its weight and interference with locomotion. It proved to be a cystic fibroma 7½ inches long and 17½ inches in circumference.

Valude [135] removed a large tumor from the right labium majus of a patient, aged 45, para-III, who had first noticed the swelling eight years previously. Its growth had been more rapid during the last 18 months. Microscopic diagnosis, fibromyoma.

Van der Smissen [136] removed a pedunculated fibroma from the right labium majus of a virgin, aged 20. The tumor was the size of a dove's egg. Two years later he delivered the patient of a child at term and noticed five small fibromata which had developed in the left labium majus.

Villiers, de Hotman and Damage [139] describe a case of calcified fibroma the size of a hen's egg, removed from the upper portion of the right labium majus of a patient, aged 61. The tumor had caused retention of urine by compression of the urethra.

Zangemeister [142] removed a tumor the size of a potato from the left labium majus of a patient, aged 36, para-I. The patient had noticed it for 10 months. Microscopic diagnosis, fibromyoma.

Zielewicz [144] describes a sessile fibroma of the labium majus, occurring in a pregnant woman, which measured 59 cm. in circumference and weighed 2965 gm.

Zubrycki.[146] A patient, aged 38, para-VI, had noticed a small tumor of the left labium majus for four years. During the last pregnancy it had increased to the size of an apple, and had become pedunculated. Microscopic diagnosis, fibroma.

B. Origin in the Labium Minus.

Baer.[9] A patient, aged 39, para-IV, had noticed, four years before, two small growths, each about the size of a mulberry, on either side of the clitoris. A few months later a number of similar growths appeared on both labia minora, and later still, the vaginal orifice, the perineum and anal orifice became similarly involved. All the growths were pedunculated. Microscopic examination proved them to be fibromata. They were composed entirely of connective tissue and showed nothing in common with skin papillomata or with elephantiasis except in macroscopic appearance.

Bell [10] removed a pedunculated growth the size of an orange from the left labium minus of a patient, aged 56, para-VI. The tumor had been present six years. Microscopic diagnosis, spindle-cell sarcoma.

Bondi [16] describes a small tumor, the size of a cherry stone, removed from the labium minus of a patient, aged 26. Histologic examination revealed the typical structure of a neurofibroma.

Bovée [17] removed a pedunculated tumor from the right labium minus of a nulliparous negress, aged 26, which proved to be a fibroma.

Burgio.[23] A patient, aged 29, had noticed a small tumor on the right labium minus for nine years. Examination showed a pinkish tumor the size of a dove's egg. Microscopic diagnosis, fibromyoma.

Collyer[29] reports a case of "fibroma diffusum" of the labia minora in a patient, aged 25, with active syphilis. Probably a case of elephantiasis.

Goldreich[56] demonstrated a case of a pedunculated fibroma of the right labium minus, the size of a hazelnut, in a baby 10 months old.

Grigorowitsch[58] describes a rare case of a woman, aged 29, showing an ulcerated tumor the size of a child's head attached to the right labium minus and a number of smaller tumors about the vaginal orifice. The principal tumor weighed 740 gm. and microscopic examination showed it to be a fibrosarcoma.

Kirchoff[72] reports a most remarkable case of a girl, aged 18, who for some years had felt, when lifting any weight, that some large object was about to come out of the vagina. One day, when lifting a heavy weight, she experienced a sudden sharp pain at the vaginal outlet accompanied by a profuse hæmorrhage. Examination showed a freshly ruptured hymen and, hanging by a thick pedicle from the right labium minus, a large tumor reaching the middle of the thigh. The tumor mass was made up of a large number of fibroid nodules.

Legneu et Morel[79] report a case in which a very œdematous fibroma was removed from the right labium minus of a patient, aged 25, in the sixth month of pregnancy. It had been present one year but had recently grown very rapidly.

Prokess[100] removed a fibroma half the size of a man's fist from the labium minus of a patient, aged 38.

C. Origin in the Submucous Connective Tissue of the Vestibule and Vagina.

Churchill[26] removed a fibrolipoma situated just below the orifice of the urethra. The tumor measured 1 inch long and ½ inch thick.

Hasenbalg ("Zwei seltene Tumoren der weiblichen Geschlechtsorgane," Zeitschr. f. Geb. u. Gyn., 1892, Bd. 23, p. 52). A tumor, which proved to be an œdematous fibroma, was found to fill the posterior vaginal vault to which it was attached by a pedicle. The patient was a virgin, aged 49.

Elischer ("Ein Fall eines Scheidenfibroms," Cent. f. Gyn., 1893, Bd. 17, p. 846). A fibromyoma the size of a date was removed from the left side of the vagina of a nullipara, aged 40.

Parsons[102] reports a case of a woman, aged 30, showing a walnut-sized tumor of the vestibule projecting forward and pushing the urethra downward. The mass proved to be a fibromyoma undergoing hyaline degeneration and containing a small calcareous nodule.

Thomass[122] removed a sessile tumor measuring 4.5 by 3 by 2.5 cm. from between the urethra and labium minus of a nullipara, aged 17. It had been noticed only three months. Microscopic diagnosis, fibroma.

D. Origin in the Subcutaneous Tissue of the Perineum.

Newman.[86] A patient, aged 30, para-V, with a pedunculated tumor of the perineum the size of a fœtal head, stated that it had grown very rapidly during her last pregnancy. On removal it proved to be a fibroma.

GROUP II. FIBROID TUMORS ORIGINATING IN THE EXTRAPERITONEAL PORTION OF THE ROUND LIGAMENT.

The development of fibroid tumors in the extraperitoneal portion of the round ligament is not especially rare. Tumors developing in this region are among the most interesting of the benign vulval growths and have received considerable comment in the literature since attention was first drawn to them by Sänger[117] in 1880. The tumor appears first in the inguinal region and as it increases in size usually pushes forward into the labium majus and becomes pedunculated. It may remain in the inguinal region indefinitely, and be partially or completely reducible. On the other hand it may in rare instances grow backward through the internal abdominal ring (Nebesky[94] and Prang[107]), or upward "between the layers of the abdominal wall" (Leopold[80]).

As might be expected, a tumor originating in this portion of the round ligament is often found in association with an inguinal hernia. Fibroids of this origin show the same marked tendency towards sarcomatous change as noted in those originating in the subcutaneous connective tissue. Of the 39 cases in Group II, five cases, or 13 per cent, showed a malignant metamorphosis.

The following cases fall naturally into two main groups according to their mode of growth:

A. Growing Outward into the Labium Majus.

Aschoff.[3] A patient, aged 42, had noticed a small tumor in the upper end of the labium for a year and a half. At operation, an adenofibroma the size of an almond was removed from the inguinal canal.

Aumoine.[7] Case (a). A patient, aged 26, para-I, had noticed a nut-sized tumor in the right inguinal region six months after her delivery, two and a half years previously. It had grown slowly into the upper end of the labium majus and had become pedunculated. It would become quite painful during menstruation. At operation, the tumor was found to arise in the round ligament and microscopic examination showed it to be a fibroma.

Aumoine.[7] Case (b). A patient, aged 45, had noticed a slow-growing, pedunculated tumor of the right labium majus for four and a half years. Operation was refused but the author considered it to have originated in the extraperitoneal portion of the round ligament.

Blisner[14] removed a fibromyoma the size of an apple from the left labium majus of a patient who had noticed the growth only a few months before. It had taken origin in the extraperitoneal portion of the round ligament.

Bochenski[19] removed a large fibroma from the right labium majus and found it attached to the round ligament. It recurred after several years.

Clark[27] describes the case of a woman, aged 59, para-IX, who showed a tumor of the uterus and a firm, circumscribed, sausage-shaped mass in the left inguinal region projecting downward into the labium along the course of the round ligament. The mass was movable, but could not be pushed back into the abdomen. At operation a hysterectomy was completed and the inguinal tumor removed through a separate incision. The tumor of the uterus proved to be a round-cell sarcoma and the inguinal mass a fibromyoma of the round ligament measuring 8 by 6 by 4 cm.

Coates.[28] A patient, aged 21, para-I, had noticed an enlargement of the upper end of the left labium majus since her earliest recollection. Before marriage it had given no discomfort whatever but was now causing pain at coition. On examination a mass was found occupying the labium and inguinal canal and extending down to the anus. It bore a remarkable resemblance to a large scrotum and on palpation two ovoid tumors the size and consistency of testicles were made out. In fact, her physician had previously made a diagnosis of hermaphroditism and only marriage disclosed her true sexual identity. At operation a multinodular tumor measuring 17 by 8 by 6 cm., and attached to the round ligament, was removed. Microscopic diagnosis, fibromyoma.

Cullen.[20] A patient, aged 37, had noticed a tumor in the upper end of the right labium majus for a number of years, which had caused pain in the inguinal region at each menstruation. At operation a tumor of the extraperitoneal portion of the right round ligament was removed, which proved, on microscopic examination, to be an adenofibroma. Two years later the patient returned with a tumor in the left iliac region and laparotomy revealed an adenofibroma of the intraperitoneal portion of the left round ligament.

Duplay.[37] A patient, aged 52, para-I, had not menstruated for seven months. Eight months before she had noticed a small, rapidly growing tumor in the right inguinal region. Examination showed a tumor in the right labium majus the size of an ostrich's egg. On removal, it proved to be fibromyoma originating in the right round ligament and showing extensive myxomatous change.

Gemmel[52] removed a fibroma the size of an orange from the labium majus of a patient, aged 44, para-X. At operation, the tumor showed considerable diffuse extension toward the inguinal canal and buttock. Microscopic examination showed the central portion of the tumor to be undergoing "a degeneration closely simulating sarcomatous change."

Géroulanos[53] reports a case in which a huge pear-shaped fibromyoma, weighing 8500 gm., hung to the knees by a thin pedicle attached to the labium majus. The tumor had probably taken origin in the extraperitoneal portion of the round ligament.

Guinard.[59] A multipara, aged 35, had noticed a multinodular tumor in the left inguinal region for 15 years. It had gradually grown downward into the labium majus. At operation a multinodular fibromyoma the size of an apple was removed from the extraperitoneal portion of the round ligament.

Hecker[64] reports the case of a patient, aged 40, who since early childhood had noticed a small tumor in the upper end of the right labium majus. It would become sensitive during menstruation. At operation, a myoma of the right round ligament, in association with a congenital hernia of the right ovary, was found.

Landau.[72] A patient, aged 59, para-II, had noticed a small nodule in the upper end of the left labium majus 20 years before. Examination revealed an enormous tumor of the labium hanging down to the knees, and measuring 65 cm. in circumference, in association with a large inguinal hernia which occupied the upper portion of the mass. Microscopic diagnosis, fibrolipoma.

Merkel[85] describes the case of a nullipara, aged 20, with a tumor the size of two fists, hanging to the middle of the thigh by a pedicle which issued from the left inguinal canal. It had been present 10 years. Microscopic diagnosis, myoma.

Morestin[88] removed a tumor of 15 years' duration from the left labium majus of a patient, aged 50. At operation, the pedicle, which was about the thickness of a finger, was found to arise in the inguinal canal. Microscopic diagnosis, fibromyoma.

Nebesky[94] (a). A patient, aged 40, para-VII, had noticed a tumor in the left labium majus 13 months before. At operation, a tumor the size of an apple, with a pedicle entering the left inguinal canal, was removed. Microscopic diagnosis, fibromyoma.

Paletta[99] removed a tumor the size of a fist from the upper portion of the left labium majus. The pedicle entered the inguinal canal and was attached to the round ligament. It contained a cystic cavity filled with clear limpid fluid. Microscopic diagnosis, fibroma.

Polaillon[105] describes the case of a multipara, aged 45, showing a pedunculated tumor of the left labium majus the size of a child's head and hanging to the middle of the thighs. The pedicle entered the inguinal canal. Microscopic diagnosis, fibromyoma.

Reboul.[110] A patient, aged 45, para-III, had noticed a small tumor the size of a pigeon's egg, in the upper part of the right labium majus, for 16 years. At menstruation, the tumor would become swollen and sensitive. At operation, a vascular fibromyoma of the extraperitoneal portion of the round ligament was found in association with a hydrocele of the canal of Nuck.

Von Recklinghausen[111] removed an adenofibroma of the extraperitoneal portion of the right round ligament of a patient, aged 49, para-V, who had complained of a tumor of the labium majus for a year and a half. It would become swollen and sensitive during menstruation and had previously been diagnosed as a hernia. It measured 3 by 3 by 2 cm.

Reverdin and Buscarlet.[113] A patient, aged 49, para-VII, had first noticed a tumor in the left labium majus the size of a nut. When seen, it had reached the size of a hen's egg and from its position and character on palpation appeared as a Bartholin gland cyst. At operation a fibromyoma, originating in the round ligament, was found.

Roustan[116] removed a fibromyoma the size of an apple, from the left labium majus of a patient, aged 42, para-VII. The tumor was of 13 months' duration. It was found to have arisen in the extraperitoneal portion of the round ligament.

Weber.[149] Case (a). A patient, aged 58, had noticed a small hard tumor in the left inguinal region three years before. It had grown to the size of a goose's egg and had invaded the labium majus. A fibroma of the left round ligament was removed.

Weber.[149] Case (b). A young nullipara had noticed a tumor in the left inguinal region three years before, which had grown rapidly and become pedunculated. At operation it was found to have originated in the extraperitoneal portion of the round ligament. Microscopic examination showed the smaller part of the tumor, near the inguinal ring, to be a myoma, while the larger, more superficially situated portion, was a myosarcoma. The sarcomatous change was traced back to trauma.

B. Remaining in the Inguinal Canal.

Doormann.[35] During her last pregnancy, five years before, a patient, aged 32, para-II, had noticed a small swelling in the right inguinal region. For three years she had worn a truss to hold it back. At operation, a fibroma of the round ligament, the size of an apple, was removed. It contained a number of cystic cavities filled with clear fluid.

Fischer.[42] A nullipara, aged 24, had noticed a slowly growing tumor in the right inguinal region for a year and a half. It had become quite painful, especially during menstruation. At operation a fibroma of the round ligament was removed.

Hansemann[62] demonstrated a case showing a myoma of the right round ligament in an inguinal hernia.

Heydemann.[63] A patient, aged 44, para-II, had noticed a tumor in the right inguinal region for a year. It would become very sensitive during menstruation. A diagnosis of irreducible inguinal hernia was made, but operation revealed a fibromyoma of the round ligament.

Hofmorkl[66] reports the case of a woman, aged 33, para-I, with a large, left-sided inguinal hernia near which a large hard tumor had appeared, causing gangrene of the overlying abdominal wall and the projecting parts. There was also a small pedunculated tumor of the left labium majus quite separate from the other mass. At operation, the larger tumor proved to be a fibroma of the left round ligament in association with an inguinal hernia. The small tumor was a fibroma of doubtful origin.

Von Mars.[85] A patient, aged 28, para-III, had noticed a painful point in the right inguinal region three years before. A year later a small tumor appeared which then grew rapidly. At operation, a fibromyoma the size of an ostrich's egg was removed from the inguinal region. The center of the tumor showed myxomatous change.

Rosinski[133] removed a tumor the size of an egg from the left inguinal region of a patient, aged 54. A half a year later he

removed a cystic tumor the size of a plum from the left inguinal region of the same patient. Both tumors were attached to the round ligament and both proved, on microscopic examination, to be adenomyoma.

Sänger.[117] A patient, aged 22, para-III, had had a swelling the size of a pigeon's egg in the right inguinal region for a number of years. It had been diagnosed a hernia. During the last three or four months, in connection with pregnancy, the tumor had increased rapidly in size. At operation a fibrosarcoma was removed which had originated in the extraperitoneal portion of the right round ligament.

Spencer-Wells.[126] Case (a). A patient, aged 50, had noticed a slowly growing, hard tumor in the right inguinal region for a year. A fibroma of the right round ligament, the size of a cocoanut, was removed.

Spencer-Wells.[126] Case (b). A patient, aged 40, had noticed a slowly growing, hard tumor in the right inguinal region for three years. A fibroma of the round ligament, the size of an orange, was removed.

Verneuil.[128] A patient, aged 26, para-I, noticed a small hard tumor in the right inguinal region six weeks after delivery. It grew very slowly and was painful only at the time of menstruation. It was diagnosed a hernia of the ovary or a hydrocele of the canal of Nuck. At operation, a fibroma was found springing from the round ligament.

Nebesky [94] and Prang [107] have each reported a case of a fibroma arising in the extraperitoneal portion of the round ligament and then growing back into the abdomen, instead of forward into the labium majus, as is usual; while Leopold [56] has reported a case in which such a tumor grew upward "between the layers of the abdominal wall." As these can hardly be considered vulval tumors they will not be reported.

GROUP III. FIBROID TUMORS ORIGINATING IN THE SUBPERITONEAL CONNECTIVE TISSUE AND APPEARING AT THE VULVA.

Subperitoneal fibromata are the largest tumors known to pathology. The largest ever reported weighed 268 pounds (Buckner [19]). The entire subject, including this case, was admirably reviewed by Whitney and Harrington [141] in 1905.

These tumors develop in the retroperitoneal connective tissue of the pelvis and growing along lines of least resistance are usually first noticed in the region of the labium majus. Later they are often complicated by further growths in the ischiorectal region, buttock or groin. More often than not there is more than one growth and it has been noted that in these cases each tumor possesses a pedicle which may be followed up along the vagina or through one of the bony foramina to a common point of origin in the subperitoneal connective tissue of the pelvis.

Clinically, these cases may be considered vulval fibroids, although they do not originate in the connective tissue of the vulva. In each of the following cases the tumor first noticed was a vulval tumor.

Bigelow.[12] A patient, aged 31, had noticed a swelling in the left groin two years previously, which had gradually grown downward, invading the left labium majus and buttock. Examination showed a lobulated tumor the size of a cocoanut occupying the left labium and buttock and extending up the vagina to the cervix. Microscopic diagnosis, fibroma.

Czyzewicz [31] removed a small myxofibroma from the region of the mons Veneris of a patient, aged 40. Eight years later she returned with a large firm tumor of the abdominal wall, extending from the symphysis to the umbilicus. It had been present one year. Microscopic examination showed it to be a fibromyoma.

Edge [38] removed a firm tumor from the left labium majus and ischiorectal fossa of a patient, aged 35. The tumor was the size of an orange, reached up to the uterus and proved on microscopic examination to be a fibroma.

Esmarch.[40] In 1872, a patient, aged 30, noticed a small swelling in the left labium majus which gradually increased in size. Three years later another tumor appeared in the right buttock and a third in the right groin. In 1876, examination showed: (a) A firm elastic tumor of the right labium majus, the size of a child's head, with a pedicle reaching up into the pelvis along the vaginal wall. (b) A similar tumor hung from the right buttock by a thick pedicle, this mass being the size of a man's head. (c) In the right inguinal region there was an irreducible tumor, the size of a fist, lying above Poupart's ligament. An attempt was made to remove the tumors of the buttock and labium but was unsuccessful. However, they were shown to be composed of myxomatous tissue. In 1877, the tumor of the right groin, which had recently grown rapidly, was removed, and a pedicle, two finger-breadths thick, which extended toward the peritoneum, was cut off as high as possible. In 1886, nine years later, and 14 years after the first tumor was noticed, the patient returned with a recurrence of the tumor of the groin, now in association with an inguinal hernia. The tumor of the buttock now hung below the knees and measured 62 cm. in circumference. The tumor of the labium had grown to the size of a man's head.

Fleming [43] operated on a patient, aged 20, for a tumor of the upper end of the right labium majus which had first been noticed four months previously. The tumor was separated from the wall of the vagina and the labium, but a considerable portion was found "passing up toward the sacro-sciatic ligament." A section showed it to be a "fibro-cellular tumor."

Gallet [48] describes a case occurring in a woman, aged 38, with a firm tumor occupying the whole left labium majus, a similar tumor the size of a man's head on the left buttock and just above it a third, smaller tumor of the same nature. At operation, the vulval growth was found to spring from a pedicle which continued up beneath the ramus of the pubes. The smaller growth on the buttock was found to be lobulated and to be attached to a pedicle which entered the obturator foramen. The largest tumor weighed 1800 gm. The patient died and at autopsy the pedicles of all three tumors were found to connect with a similar tumor in the left side of the pelvis, which was not connected with the pelvic organs in any way. Section showed the tumors to be fibromata containing many small cystic cavities.

Harrington [63] removed a pedunculated fibroma, the size of a fœtal head at term, from the left labium majus of a patient, aged 46. Six years later the patient returned with a smaller tumor hanging from the left labium and a pedunculated tumor of the same nature hanging from the left buttock and measuring 18½ inches in circumference. The patient was suffering from retention of urine. A catheter showed the bladder to be drawn over toward the large posterior tumor. Both tumors were removed and at the end of five years there had been no recurrence. Microscopic diagnosis, fibroma.

Kaan.[69] A patient, aged 20, para-II, had noticed a slowly growing tumor in the left labium majus for five years. Examination showed a tumor the size of a fist, hanging between the thighs and a portion of it extending up the left side of the vagina into the pelvic cavity, where it was connected with a mass the size of a six months' pregnancy. At autopsy, the growth was found to have taken its origin in the subperitoneal connective tissue. Microscopic diagnosis, œdematous fibroma.

Kuster.[74] A patient, aged 42, had noticed a small nodule in the left labium majus and two nodules the size of hazelnuts, just to

the left of the anus, one year previously. Their growth had been so rapid that locomotion was now interfered with. Examination revealed a large soft tumor of the labium which was definitely lobulated and could be followed to the anus. Microscopic diagnosis, fibroma.

MacEwen [83] removed a tumor weighing three pounds from the left labium majus of a patient, aged 49, para-IX, which had been present nine years. The author considered it to have originated in the ischiorectal fossa and to have extended from there into the labium and also upward, perforating the levator ani muscle and fascia, and then growing in front of the bladder. Microscopic diagnosis, œdematous fibroma.

Malcolm [84] describes the case of a patient, aged 30, para-I, with three large fibroid tumors, all uniting in the left side of the pelvis. There was, first, a tumor 7½ inches long distending the perineum; second, a tumor of the buttock 37½ inches long; and third, a large, ill-defined abdominal tumor. The peritoneal tumor was found to be "firmly fixed to the fascia covering the muscles of the anterior lateral wall of the pelvis" and for this reason the author considers it to have taken origin in the fascial tissue. (On account of the typical description given, I feel justified in including this case among the subperitoneal tumors.)

Von Langenbeck.[77] Case (a). A patient, aged 20, noticed a lump the size of a hazelnut in the right labium majus following trauma. Three years later she had a growth the size of a man's head in the labium and perineum, compressing the vagina and rectum and extending up into the pelvis. In extirpating it a small piece was left adherent to the peritoneum above. The rectum and vagina were intimately adherent. Microscopic diagnosis, œdematous fibroma.

Von Langenbeck.[77] Case (b). A patient, aged 36, first noticed a small tumor of the perineum which had grown to the size of two fists within a year. It was found to be distending the perineum, the lower portion of the right labium majus and the adjacent skin of the thigh. The vagina was pushed to the left and the tumor was found to extend up into the pelvis. At operation it was necessary to dissect it from the vagina and rectum. Microscopic diagnosis, œdematous fibroma.

Sympson [120] removed a tumor weighing one pound three ounces from a woman, aged 43, who had noticed it for 18 months. One process passed forward along the vagina into the labium majus and another, upward and backward, very deeply along the rectum, to which it was attached. It was also atttached to the sacrosciatic ligament and to the coccyx. It measured 9 by 4 inches. Microscopic diagnosis, fibroma.

The following cases are of interest as vulval fibroids, but it is questionable whether separate groups should be made of them. Fromme [46] describes a large tumor of the labium majus which proved to be a fibromyoma containing glandular elements and which he considers to have originated in Bartholin's gland. In this connection it should be remembered that an adenomyoma of the extraperitoneal portion of the round ligament may grow outward, into the labium majus, and appear as a labial growth. Morestin [92] has advanced the view that a fibroma may develop during the organization of a hematoma, while Kewisch [73] claims that they may develop from either the pelvic fascia or the periosteum of the pelvic bones. The connective tissue of the rectovaginal septum has also been noted as a point of origin. It cannot be denied that these are possibilities, but cases which might be considered as belonging to these groups are very rare.

The following cases have been reported:

GROUP IV. FIBROID TUMORS ORIGINATING IN THE CONNECTIVE TISSUE OF BARTHOLIN'S GLAND.

Fromme.[46] A patient, aged 18, had noticed a small tumor of the right labium majus a year and a half previously. During the last six months it had grown to the size of a fist. Examination showed a large bluish mass occupying the entire right labium, and forcing the vaginal outlet to the left. It lay immediately beneath the skin. Microscopic examination revealed a connective-tissue tumor containing a few smooth muscle fibers and some fat. Single tubular glands were scattered throught the entire growth. They were lined with a single layer of epithelium and gave evidence of being offshoots of Bartholin's gland.

Lala [75] reports a tumor of the right labium majus, which from its situation may have been a case similar to that of Fromme. The tumor, "chiefly of fibro-plastic tissue," was "encysted" in the right labium majus and obstructed the vagina.

Piering [109] removed a rather soft tumor the size of a man's fist which occupied the position of the right Bartholin gland and preceded, for some years, an abscess of the gland. Microscopic examination showed a very cellular fibroma in which there was a single area of hyaline degeneration. This tumor may have originated in the subcutaneous tissue.

Von Recklinghausen [113] removed a tumor of Bartholin's gland which showed a marked thickening of the interstitial connective tissue.

GROUP V. FIBROID TUMORS ORIGINATING IN HÆMATOMATA.

Demarquay [34] removed a fibrolipoma from the labium majus which had developed after trauma to that labium. The tumor had begun to increase in size and become painful at the time of menstruation.

Morestin [92] reports a case in which a fibroma the size of a hen's egg developed in a hæmatoma in the right labium majus, following trauma. The appearance was remarkably like that of a scrotum.

These two cases may, of course, be considered as belonging to Group I.

GROUP VI. FIBROID ORIGINATING IN THE RECTOVAGINAL SEPTUM.

Bryant.[18] A patient, aged 40, had had a painless tumor at one side of the perineum, for two years. At operation it was found to be compressing both the vagina and rectum and was enucleated from between them. The tumor was 6 inches long and proved to be an œdematous fibroma.

Smith [124] removed a soft fibroma the size of a goose's egg from the perineum of a woman, aged 37, para-II. It was firmly embedded in the rectovaginal septum, weighed four ounces, and one process was adherent to the rectum for five inches. Another prolongation was adherent to the vagina.

SUMMARY.

Fibroid tumors of the vulva are the commonest of the benign solid tumors of this region and grow to larger size than superficial fibroid tumors in any other part of the body. As a rule they grow rapidly and soon become pedunculated. Most of them show some form of degenerative change.

The subperitoneal fibromata, which take origin in the pelvic connective tissue and, growing along lines of least resistance, first appear at the vulva, are the largest tumors on record. The

largest tumor ever described was one of this type (Buckner,[19] Whitney and Harrington [20]), and weighed 268 pounds.

Excluding the subperitoneal group, it may be said that, roughly, two-thirds of the fibroids of the vulva originate in the subcutaneous connective tissue and one-third in the extraperitoneal portion of the round ligament, *while nearly one-fifth of them become sarcomatous.*

The vascular changes accompanying menstruation and pregnancy are shared by these tumors and exert a marked influence upon them, as is clearly shown by their swelling and sensitiveness under these circumstances. Herein lies the explanation of the fact that, almost without exception, they occur in the child-bearing period, that they grow rapidly, that they usually show degenerative changes and, finally, that a remarkably large percentage of them become sarcomatous.

I wish to take this opportunity to express my appreciation to Dr. Howard A. Kelly, not only for the privilege of reporting these cases, in whose clinic at The Johns Hopkins Hospital they occurred, but mainly for the inspiration and stimulus which the years of close association with his untiring work have always meant to his assistants.

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FIG. 1.—Case I. Pedunculated fibroma of the labium majus.

FIG. 2.—Case III. Pedunculated fibroma of the labium majus.

FIG. 3.—Case IV. Section of a fibromyxosarcoma of the labium majus.

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INDEX TO VOLUME XXVIII OF THE JOHNS HOPKINS HOSPITAL BULLETIN.

Abstracts of papers representing work done in The Johns Hopkins Hospital, but published elsewhere than in the BULLETIN: Barker, L. F. and Hodge, M., On the control of diabetes insipidus by means of hypophyseal extract in a multiglandular endocrinopathy (thyreo-hypophyseo-genital syndrome), 355;—Barker, L. F. and Mosenthal, H. O., On the effects of injection of hypophyseal extracts (posterior lobe and pars intermedia) in the treatment of diabetes insipidus, 355;—Barker, L. F. and Sprunt, T. P., On a regimen that has been found helpful in the treatment of some cases of so-called pernicious anæmia, 355;—Burns, J. E., Further observations on the use of thorium in pyelography, 181;—Burrows, M. T., Some factors regulating growth, 269; The significance of the lunula of the nail, 268; The tissue culture in cancer, 269;—Burrows, M. T., Burns, J. E. and Suzuki, Y., Cultivation of bladder and prostatic tumors outside the body, 178;—Burrows, M. T. and Neymann, C. A., The toxicity of α-amino-acids for embryonic chicken cells, 180;—Cobb, S., Bailey, A. A. and Holtz, P. R., On the genesis and inhibition of extensor rigidity, 357;—Conrad, H. B., A case of pneumonia of unusually short duration, 357;—Davis, D. M., The effect of calcium, water and other substances given intravenously, on blood composition and urinary secretion, 177;—Davis, D. M. and Gorton, W. S., A modified Woodyatt pump, 178;—Davis, D. M. and Rosen, R., Surface sterilization of tissue for bacterial studies, 272;—Davis, J. S., A comparison of the permanence of free transplants of bone and cartilage, an experimental study, 267;—Some of the problems of plastic surgery, 356;—Mosenthal, H. O. and Hiller, A., The relation of the non-protein nitrogen to the urea nitrogen of the blood, 179;—Neymann, C. A., Some experiences in the German Red Cross, 359;—Sydenstricker, V. P. W., Mason, V. R. and Rivers, T. M., Transfusion of blood by the citrate method, 271;—Young, H. H. and Davis, E. C., Double ureter and kidney, with calculous pyonephrosis of one-half; cure by resection. The embryology and surgery of double ureter and kidney, 176.

Adenomyoma of the recto-vaginal septum, 343.

Apoplexy, A contribution to the pathology of, Multiple spontaneous intracerebral hæmorrhages, 86.

Baer, W. S., Sacro-iliac strain, 159.

Blood, circulating, The cultivation of tubercle bacilli from the, in miliary tuberculosis, 363.

Blood picture, Changes in the, after nucleic acid injections, 146.

Blood-sugar, The obstetrical significance of the, with special reference to the placental interchange, 140.

Blood, The amino-acid of the, in cases of normal and complicated pregnancy and also in the newborn infant, 199.

Blood, Transfusion of. History, methods, dangers, preliminary tests, present status. Report of 150 transfusions, 99.

Bloomfield, A. L., The effects of serum therapy in acute lobar pneumonia, 301.

Books received: 98; 186; 275; 334; 362; 385.

Brown, N. W., The fasciolopsinæ of China: a study of two specimens from Chekiang province, 322.

Bunting, C. H. and Yates, J. L. Leukæmia, pseudoleukæmia and Hodgkin's disease, 151.

Cæsarean section, A histological study of 50 uteri removed at, 335.

Campbell, C. M., On the mechanism of convulsive phenomena and allied symptoms, 318.

Carrel treatment of wounds applied to civil practice, 294.

Cerebrospinal fluid, The significance of xanthochromia of the, 80.

Clough, M. C., A study of the incidence of the types of pneumococci isolated from acute lobar pneumonia and other infections, and an analysis of the cases classified by types in regard to mortality, complications, associated diseases, bacteriæmia and leucocytosis, 306.

Clough, M. C., The cultivation of tubercle bacilli from the circulating blood in miliary tuberculosis, 363.

Convulsive phenomena and allied symptoms, On the mechanism of, 318.

Crowe, S. J., Watkins, S. S. and Rothholtz, A., Relation of tonsillar and nasopharyngeal infections to general systemic disorders, 1.

Cullen, T. S., Adenomyoma of the recto-vaginal septum, 343.

Diabetes mellitus, The D:N ratio in, 187.

Discussion: Johns Hopkins Hospital Medical Society: Baer, W. S., The recent epidemic of infantile paralysis, 135;—Barker, L. F., Exhibition of a case of gigantism in a girl 12 years of age, 96; Experiences with acoustic tumors, 239;—Blake, J. D., The recent epidemic of infantile paralysis, 135;—Cushing, H., Experiences with acoustic tumors, 239;—Emerson, H., The recent epidemic of infantile paralysis, 136;—Evans, F. A., Anatomical changes associated with high cholesterin diet, 211;—Ford, W. W., Observations bearing on the possibility of developing an experimental chemotherapy of tuberculosis, 124;—Fulton, J. S., The recent epidemic of infantile paralysis, 135;—Halsted, W. S., Experi-

ences with acoustic tumors, 239;—Heuer, G. J., Experiences with acoustic tumors, 239;—Howell, W. H., Regeneration in peripheral nerves. An experimental study, 79;—Janeway, T. C., The recent epidemic of infantile paralysis, 134;—Krause, A. K., The mechanism and clinical significance of anaphylactic and pseudoanaphylactic skin reactions, 173;—Livingston, B. E., Is there any real analogy between crown gall and cancer? 209;—Smith, E. F., Is there any real analogy between crown gall and cancer? 210;—Thayer, W. S., Exhibition of a case of gigantism in a girl 12 years of age, 96;—Is there any real analogy between crown gall and cancer? 210;—Welch, W. H., Experiences with acoustic tumors, 239;—Winternitz, M. C., Is there any real analogy betwen crown gall and cancer? 210.

Discussion: Laennec Society: Austrian, C. R., Chronic non-tuberculous lung infection, 213;—Baetjer, F. H., The rœntgen diagnosis of pulmonary tuberculosis, 333;—Boggs, T. R., Chronic non-tuberculous lung infection, 214;—Bronfenbrenner, J., Complement fixation in tuberculosis, 244;—Garvin, A. H., Chronic non-tuberculous lung infection, 215;—Hamman, L., The rœntgen diagnosis of pulmonary tuberculosis, 333;—Janeway, T. C., Chronic non-tuberculous lung infection, 215;—Krause, A. K., Chronic non-tuberculous lung infection, 214;—Leutscher, J. A., Chronic non-tuberculous lung infection, 214;—Miller, H. R., Complement fixation in tuberculosis, 244;—Penrose, C. A., Chronic non-tuberculous lung infection, 214;—Petroff, S., Complement fixation in tuberculosis, 243;—Wilson, Gordon, Chronic non-tuberculous lung infection, 214.

Dunn, G. R. and McClure, R. D., Transfusion of blood. History, methods, dangers, preliminary tests, present status. Report of 150 transfusions, 99.

Embryomas in plants (produced by bacterial inoculations), 277.

Emerson, H., The recent epidemic of infantile paralysis, 131.

Fasciolopsinæ of China: a study of two specimens from Chekiang province, 322.

Ford, W. W. and Lawrence, J. H., Hæmolytic substances in heated milk and in milk cultures of Bacterium welchii, 245.

Friedenwald, H., The ethics of the practice of medicine from the Jewish point of view, 256.

Greenacre, P., Multiple spontaneous intracerebral hæmorrhages. A contribution to the pathology of apoplexy, 86.

Hæmatomata of the ovary, including corpus luteum cysts, 349.

Hæmorrhages, Multiple spontaneous intracerebral. A contribution to the pathology of apoplexy, 86.

Harlan, H. D., Presentation of the medallion portrait of Dr. Rupert Norton, 230.

Howard, C. P. and Ingvaldsen, T., The mineral metabolism of experimental scurvy of the monkey, 222.

Hurd, H. M., Johns Hopkins and some of his contemporaries, 225;—Presentation of the medallion portrait of Dr. Rupert Norton, 229.

Ingvaldsen, T. and Howard, C. P., The mineral metabolism of experimental scurvy of the monkey, 222.

Johns Hopkins and some of his contemporaries, 225.

Kidney, On the etymology, popular and scientific, of the terms for, in various languages, 204.

King, J. T., Jr., Aleucocythæmic leukæmia. 1. Acute myeloblastic leukæmia. 2. Chloroma (?). 3. Chronic lymphatic leukæmia, 114.

Kirk, E. G. and Lewis, D. D., Regeneration in peripheral nerves. An experimental study, 71.

Klebs, A. C., Paleopathology, 261.

Kolmer, J. A., The mechanism and clinical significance of anaphylactic and pseudoanaphylactic skin reactions, 163.

Krause, A. K., The nature of resistance to tuberculosis, 191;—Undergraduate instruction in tuberculosis, 217.

Lawrence, J. S., The Carrel treatment of wounds applied to civil practice, 294.

Lawrence, J. S. and Ford, W. W., Hæmolytic substances in heated milk and in milk cultures of Bacterium welchii, 245.

Leonard, V. N., Fibroid tumors of the vulva, 373.

Leukæmia, Aleucocythæmic. 1. Acute myeloblastic leukæmia. 2. Chloroma (?). 3. Chronic lymphatic leukæmia, 114.

Leukæmia, pseudoleukæmia and Hodgkin's disease, 151.

Lewis, D. D. and Kirk, E. G., Regeneration in peripheral nerves. An experimental study, 71.

Lewis, D. S. and Mosenthal, H. O., The D:N ratio in diabetes mellitus, 187.

Lewis, P. A., Observations bearing on the possibility of developing an experimental chemotherapy of tuberculosis, 120.

Macht, D. I., On the etymology, popular and scientific, of the terms for kidney in various languages, 204.

Marcy, C. H. and White, W. C., Tuberculosis of the tongue. Specific cure, 174.

McClure, R. D. and Dunn, G. R., Transfusion of blood. History, methods, dangers, preliminary tests, present status. Report of 150 transfusions, 99.

Medical profession of the United States, An appeal to the, 276; 300; 334.

Medicine, How Constantine the African brought the art of, to the Christians. A legend of Salerno, 64.

Medicine, The ethics of the practice of, from the Jewish point of view, 256.

Milk, heated, Hæmolytic substances in, and in milk cultures of Bacterium welchii, 245.

Morriss, W. H., The obstetrical significance of the blood-sugar with special reference to the placental interchange, 140.

Morse, A., The amino-acid nitrogen of the blood in cases of normal and complicated pregnancy and also in the new-born infant, 199.

Mosenthal, H. O. and Lewis, D. S., The D:N ratio in diabetes mellitus, 187.

Nasopharyngeal and tonsillar infections, Relations of, to general systemic disorders, 1.

Nerves, peripheral, Regeneration in. An experimental study, 71.

Neymann, C. A., Changes in the blood picture after nucleic acid injections, 146.

Nitrogen, The amino-acid, of the blood in cases of normal and complicated pregnancy and also in the new-born infant, 199.

Norton, Dr. Rupert, Presentation of the medallion portrait of, 229.

Notes and news, 69.

Notes on new books, 125; 158; 181; 215; 274; 299; 359;—Albee, F. H., Bone graft surgery, 185;—Berkhart, J. B., Nervous asthma. Its pathology and treatment, 299;—Berkley, C. and Bonney, V., The difficulties and emergencies of obstetric practice, 300;—Blumgarten, A. S., Materia medica for nurses, 360;—Brockbank, E. M., Practical points in the diagnosis and treatment of heart disease, 128;—Buck, A. H., The growth of medicine, 361;—Burdett, H., Burdett's hospitals and charities, 1916;—Coolidge, A., Diseases of the nose and throat, 299;—Crile, C. W., Man—an adaptive mechanism, 274;—The kinetic drive, 274;—The origin and nature of the emotions, 185;—Cunning, J. and Campbell, A., The healthy girl, 299;—Curtis, J. G., Harvey's views on the use of the circulation of the blood, 158;—Da Costa, J. C., Jr., Physical diagnosis, 183;—Davidson, J. M., Localization by X-rays and stereoscopy, 185;—De Lee, J. B., Principles and practice of obstetrics, 300;—Delorme, E., War surgery, 215;—Dutton, W. F., Hand-book of venesection, 299;—Egbert, S., Hygiene and sanitation, 125;—Eliason, E. L., Practical bandaging, including adhesive and plaster-of-Paris dressings, 185;—Elsberg, C. A., Diagnosis and treatment of surgical diseases of the spinal cord and its membranes, 185;—Faught, F. A., Blood-pressure from the clinical standpoint, 184;—Flagg, P. J., The art of anesthesia, 128;—French, R. L., Home care of consumptives,

130;—Friesner, I., Cerebellar abscess, 185;—Gee, S. J., Medical lectures and clinical aphorisms, 127;—Goddard, H. H. The criminal imbecile, 125;—Graves, W. P., Gynecology, 130;—Hare, H. A., Practical therapeutics, 361;—Harris, D. F., Nerves, 130;—Hart, T. S., The diagnosis and treatment of abnormalities of myocardial function, 361;—Hawk, P. B., Practical physiological chemistry, 127;—Hazen, H. H., Diseases of the skin, 183; Skin cancer, 184;—Horder, T., Cerebrospinal fever, 158;—Howell, W. H., A text-book of physiology for medical students and physicians, 185;—Hull, A. J., Surgery in war, 274;—International clinics, 1916, i and ii, 129; iii, 184;—Joslin, E. P., The treatment of diabetes mellitus, with observations upon the disease based upon 1000 cases, 128;—Kellogg, J. H., The new method in diabetes, 361;—La Motte, E. N., The backwash of war, 127;—Léjars, F., Urgent surgery, 184;—Lewis, T., Clinical disorders of the heart beat, 129;—Luciani, L., Human physiology, 125;—Mackenzie, J., The principles of diagnosis and treatment in heart affections, 181;—Macnamara, N. C., Instinct and intelligence, 182;—McKenzie, R. T., Exercise in education and medicine, 126;—McMechan, F. H., The American year-book of anesthesia and analgesia, 299;—McMurrich, J. P., The development of the human body, 362;—Meara, F. S., The treatment of acute infectious diseases, 130;—Morison, R. and Richardson, W. G., Abdominal injuries, 158;—Northcote, H., Christianity and sex problems, 129;—Oliver, G., Studies in blood pressure; physiological and clinical, 360;—Parker, E. M. and Breckenridge, S. D., Surgical and gynecological nursing, 129;—Peter, L. C., The principles and practice of perimetry, 182;—Power, D'A., Wounds in war: their treatment and their results, 158;—Report of the first expedition to South America, 1913, Harvard School of Medicine, 361;—Satterthwaite, T. E., Cardiovascular diseases, 360;—de Schweinitz, G. E., Diseases of the eye, 181;—Scott, R. J. E., Gould's practitioner's medical dictionary, 130;—Scott, T. B., Modern medicine and some modern remedies, 158;—Shears, G. P., Obstetrics, normal and operative, 183;—Sollman, T., A laboratory guide in pharmacology, 359;—A manual of pharmacology and its application to therapeutics and toxicology, 359;—Squier, J. E., Medical hints, 158;—Studies in surgical pathological physiology from the laboratory of surgical research, 185;—Sutton, R. L., Diseases of the skin, 129;—Underhill, Frank P., The physiology of the amino acids, 127;—Vicke, V. G., Sexual impotence, 129;—Webster, R. W., Diagnostic methods: chemical, bacteriological and microscopical, 299;—White, R. P., Occupational affections of the skin, 127;—Wood, H. C., Jr., Pharmacology and therapeutics, 360;—Zinsser; H., Hopkins, J. G. and Ottenburg, R., A laboratory course in serum study, 128.

Novak, E., Hæmatomata of the ovary, including corpus luteum cysts, 349.

Oertl, Horst, Venous congestion in its relation to necroses of the liver, 249.

Ovary, Hæmatomata of the, including corpus luteum cysts, 349.

Paleopathology, 261.

Paralysis, infantile, The recent epidemic of, 131.

Plass, E. D., Placental transmission: creatinine and creatine in the whole blood and plasma of mother and fœtus, 137.

Plass, E. D., Placental transmission: total creatinine in plasma, whole blood and corpuscles of mother and fœtus. (Additional analyses by a new method), 297.

Placental interchange, The obstetrical significance of the blood-sugar with special reference to the, 140.

Placental transmission: creatinine and creatine in the whole blood and plasma of mother and fœtus, 137.

Placental transmission: total creatinine in plasma, whole blood and corpuscles of mother and fœtus. (Additional analyses by a new method), 297.

Pneumonia, lobar, acute, The effects of serum therapy in, 301.

Pneumonia, lobar, An epidemiological study of, 312.

Pneumonia, lobar, A study of the bacteriæmia in, 315.

Pneumonia and other infections, A study of the types of pneumococci isolated from, and an analysis of the cases classified by types in regard to mortality complications, associated diseases, bacteriæmia, and leucocytosis, 306.

Pregnancy, The amino-acid nitrogen of the blood in cases of normal and complicated, and also in the new-born infant, 199.

Proceedings of The Johns Hopkins Hospital Historical Club: Boggs, T. R., Thomas Holley Chivers, medical poet, contemporary of Poe, 240;—Foote, J., Giovanni, Maria Lancisi: clinician, pathologist, epidemiologist, 331;—Garrison, F. H., The gods of the underworld in ancient medicine, 332;—Hurd, H. M., Johns Hopkins and some of his contemporaries, 331;—Klebs, A. C., Prehistoric pathology—paleopathology, 158;—Macht, D. I., On the etymology, popular and scientific, of the term for kidney in various languages, 158;—Presentation of the medallion portrait of Dr. Rupert Norton, 331;—Thomas H. M., Elizabeth Fry, Quaker philanthropist: her work for prisoners and insane, 240.

Proceedings of The Johns Hopkins Hospital Medical Society: Bayne-Jones, S., The blood-vessels of the heart valves, 212;—Brown, N. W., Demonstration of a simple method for determination of venous pressure, 331;—Burrows, M. T., The oxygen pressure necessary for cellular activity, 210; Clark, A. H., The interrelation of the surviving heart and pancreas of the dog in sugar metabolism, 211:—Cushing, H., Experiences with acoustic tumors, 238;—Dandy, W. E., Exhibition of cases, 96;—Davis, J. S., Some results of plastic surgery, 98;—Emerson, H., The recent epidemic of infantile paralysis, 153;—Felton, L. D., H-ion concentration of cerebro-spinal fluid, 210;—Goetsch, E., Adrenalin hypersensitiveness in hyperthyroidism, 331; Studies on disturbances of thyroid function, with special reference to thyroid adenomata, 331;—Henderson, L. J., Acidosis, 330;—Heuer, G. J., Exhibition of a case of gigantism in a girl 12 years of age, 96; Exhibition of a patient with a calcified cyst in the right pleural cavity, 153;—Hurwitz, S. H., Studies of the blood proteins in infection and immunity, 209;—Kolls, A. C., Demonstration of an apparatus for taking continuous blood pressure tracings in man, 212;—Kolmer, J. A., The mechanism and clinical significance of anaphylactic skin reactions, 209;—Levy, R. L., Studies on the physiology of thyroid secretion, 97;—Libman, E., Subacute streptococcus endocarditis in the bacterial and bacteria-free stages, 330;—MacCallum, W. G., Medical and other studies in the East Indies, 240;—Macht, D. I., Absorption of drugs through the eye, 330; Action of opium alkaloids on the ducts of the testis, 97; Truth and poetry concerning hydrastis, 330;—Marshall, E. K., Jr. and Kolls, A. C., The effect of unilateral excision of the adrenal, section of the splanchnic and section of the renal nerves on the secretion of the kidney, 238;—Novak, E., Hæmatomata of the ovary including corpus luteum cysts, 330;—Porter, W. T., Shock at the front, 212;—Richardson, E. H., A case of saphenous varix simulating a femoral hernia, 330;—Richardson, H. B. and Park, E. A., Demonstration of spontaneous rhythmic contraction of arteries, 331;—Rivers, T. M., Exhibition of cases, 212;—Robinson, S., The surgical treatment of bronchiectasis, 209; Schmeisser, H. C., Anatomical changes associated with high cholesterin diet, 211;—Shaw, H. N., Treatment of leucorrhœa, 330;—Shohl, A. T. and Janney, J. H., The growth of B. coli in urine at varying hydrogen-ion concentration, 330;—Sisson, W. R., A hitherto undescribed sporotrichum, 331;—Smith, Erwin, Is there any real analogy between crown gall and cancer? 209;—Sydenstricker, V. P. W., Exhibition of a case of cerebro-spinal meningitis, 329;—Welch, W. H., Medical problems of the war, 154;—Wharton, L., A

summary of end-results in the treatment of cases of pelvic abscess by vaginal incision and drainage, 330;—Williams, J. W., Exhibition of case of traumatic rupture of the symphysis pubis at the time of labor, 208;—Winternitz, M. C., Experimental nephropathy in the dog. Lesions produced by injection of the B. bronchisepticus into the renal artery, 212;—Wynne, H. M. N., Observation on the degeneration of leucocytes in the urine as a diagnostic aid in tuberculosis of the urinary tract in women, 330; Stricture of the ureter. Report of 100 cases, 331.

Proceedings of the Laennec Society: Bronfenbrenner, J., The complement fixation test in tuberculosis with Besredka's antigen, 240:—Garvin, A. H., Chronic non-tuberculous lung infections, 213:—Heise, F. H. and Sampson, H. L., A comparative analysis of roentgen ray pictures, physical signs and symptoms in pulmonary tuberculosis, 332;—Howk, H. J., The public health work of a great life insurance company, 334;—Miller, H. R., Complement fixation in tuberculosis, 242;—Miller, J. A., The social service side of tuberculosis work in New York, 334;—Pancoast, H. K., The roentgen diagnosis of pulmonary tuberculosis, 333.

Recto-vaginal septum, Adenomyoma of, 343.

Rohrer, C. W. G., Note on books given to The Johns Hopkins Hospital by Dr. Hugh H. Young, 231.

Rothholtz, A., Crowe, S. J. and Watkins, S. S., Relation of tonsillar and nasopharyngeal infections to general systemic disorders, 1.

Sacro-iliac strain, 159.

Salerno, A legend of. How Constantine the African brought the art of medicine to the Christians, 64.

Scurvy of the monkey, The mineral metabolism of experimental, 222.

Sevier, C. E. and Sutton, A. C., A study of the bacteriæmia in lobar pneumonia, 315.

Singer, C., A legend of Salerno. How Constantine the African brought the art of medicine to the Christians, 64.

Skin reactions, The mechanism and clinical significance of anaphylactic and pseudo-anaphylactic, 163.

Smith, E. E., Embryomas in plants, (produced by bacterial inoculations), 277.

Sprunt, T. P. and Walker, J. E., The significance of xanthochromia of the cerebrospinal fluid, 80.

Sutton, A. C. and Sevier, C. E., A study of the bacteriæmia in lobar pneumonia, 315.

Sutton, A. C. and Sydenstricker, V. P. W., An epidemiological study of lobar pneumonia, 312.

Sydenstricker, V. P. W. and Sutton, A. C., An epidemiological study of lobar pneumonia, 312.

Thayer, W. S., Presentation of the medallion portrait of Dr. Rupert Norton, 229.

Titles of papers appearing during the year elsewhere than in the Bulletin by present and former members of the hospital and medical school staff, 89.

Tonsillar and nasopharyngeal infections, Relation of, to general systemic disorders, 1.

Tuberculosis of the tongue. Specific cure, 174.

Tuberculosis of the urinary tract in women, Observations on the degeneration of leucocytes in the urine as a diagnostic aid in, 251.

Tuberculosis, miliary, The cultivation of tubercle bacilli from the circulating blood in, 363.

Tuberculosis, Observations bearing on the possibility of developing an experimental chemotherapy of, 120.

Tuberculosis, The nature of resistance to, 191.

Tuberculosis, Undergraduate instruction in, 217.

Tumors, Fibroid, of the vulva, 373.

Urine, Observations on the degeneration of leucocytes in the, as a diagnostic aid in tuberculosis of the urinary tract in women, 251.

Uteri, 50 removed at Cæsarean section, A histological study of, 335.

Venous congestion in its relation to necroses of the liver, 249.

Vulva, Fibroid tumors of the, 373.

Walker, J. E. and Sprunt, T. P., The significance of xanthochromia of the cerebrospinal fluid, 80.

Watkins, S. S., Crowe, S. J. and Rothholtz, A., Relation of tonsillar and nasopharyngeal infections to general systemic disorders, 1.

Welch, W. H., Presentation of the medallion portrait of Dr. Rupert Norton, 230.

White, W. C. and Marcy, C. H., Tuberculosis of the tongue, Specific cure, 174.

Williams, J. W., A histological study of 50 uteri removed at Cæsarean section, 335.

Wounds, The Carrel treatment of, applied to civil practice, 294.

Wynne, H. M. N., Observations on the degeneration of leucocytes in the urine as a diagnostic aid in tuberculosis of the urinary tract in women, 251.

Xanthochromia of the cerebrospinal fluid, The significance of, 80.

Yates, J. L. and Bunting, C. H., Leukæmia, pseudoleukæmia and Hodgkin's disease, 151.

Young, Dr. Hugh H., Note on books given to The Johns Hopkins Hospital by, 231.

ILLUSTRATIONS.

Operative technique in dissection and removal of tonsils, Figs. 9-13, 18-19.

Photographs of patients with tuberculous glands of neck (Plate I, Figs. 1-3), 24.

Tuberculous areas in tonsils (Plates II-IV, Figs. 4-8), 24-25.

Subscription of MS. British Museum, Sloane 2426, written in an early fifteenth century hand, 65.

MS. British Museum, Sloane 2426, Folio 8 verso, in an early fourteenth century hand, 66.

Regeneration in peripheral nerves (Plates V-X, Figs. 1-27), 78-79.

Diagram of the blood supply of the brain, 87.

Intrapontine hæmorrhage (Plate XI, Figs. 1-2), 88.

Aleucocythæmic leukæmia (Plates XII-XV, Figs. A-C; Figs. 1-11), 118-119.

Charts showing distribution of infantile paralysis in the various boroughs of New York City (Plates XVI-XX, Figs. 1-6), 136-137.

Changes in the blood picture after nucleic acid injections (Curves 1-6), 148-150.

Sacro-iliac strain (Plate XXI, Figs. 1-3), 162.

Tuberculosis of the tongue (Plate XXII, Figs. 1-2), 174.

Mineral metabolism of experimental scurvy of the monkey (Plate XXIII, Figs. 1-2), 224.

Johns Hopkins (Plate XXIV), 228.

Medallion portrait of Dr. Rupert Norton (Plate XXV), 230.

Diagram of structure of a tobacco stem, 288.

Embryomas in plants (Plates XXVI-LIII, Figs. 1-115), 292-293.

Epidemiological study of lobar pneumonia, 313.

The fasciolopsinæ of China (Plates LIV-LX, Figs. 1-31), 328-329

Histological study of 50 uteri removed at Cæsarean section (Plates LXI-LXIV, Figs. 1-12), 342-343.

Adenomyoma of the recto-vaginal septum (Plates LXV-LXXIX, Figs. 1-17), 348-349.

Hæmatomata of the ovary (Plates LXXX-LXXXII, Figs. 1-6), 354.

Fibroid tumors of the vulva (Plate LXXXIII, Figs. 1-3), 384.

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